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CONTENTS AND SUBJECT INDEX

Epochs in Medicine: The Improvement of Medical Service to Labor. E. E. Irons, M.D., Chicago...621

Primary Coccidioidomycosis: A Possible Pediatric Problem. Major Ralph H. Kunstadter and Major Robert C. Pendergrass, M. C., A. U. S. 624
Discussed by Major Wood.

Hemolytic Transfusion Reactions Due to Rh Incompatibility. Lawrence E. Young, M.D., and Donald H. Kariher, M.D., Rochester, N. Y. 627

Fetal Erythroblastosis. Israel Davidsohn, M.D., Chicago.....633
Discussed by Drs. Foord and Davidsohn.

Administration of Penicillin by Mouth. Paul György, M.D.; H. N. Vandegrift, M.D.; William Elias, Ph.D.; L. G. Colio, B.A., Philadelphia; F. M. Barry, M.D., and J. D. Pilcher, M.D., Cleveland.639

Curare in Anesthesia. Harold R. Griffith, M.D., Montreal.....642
Discussed by Drs. Cullen, Baird and Griffith.

CLINICAL NOTES, SUGGESTIONS AND NEW INSTRUMENTS

Fulminating Meningococcemia (Waterhouse-Friderichsen Syndrome). J. M. Hayes, M.D., Los Angeles, and John F. Whalen, M.D., Altadena, Calif.....645

Fatal Agranulocytosis Resulting from Thiouracil. M. Irene Ferrer, M.D.; David M. Spain, M.D., and Richard T. Cathcart, M.D., New York..646

Bilateral Temporal Arteritis with Complete Loss of Vision. Edward W. Shannon, M.D., Cleveland, and James Solomon, M.D., Boston..647

COUNCIL ON FOODS AND NUTRITION 649

EDITORIALS

Coordinated Research for the Testing of Antimalarial Drugs.....650

Penicillin Treatment of Virus Diseases 652

The Hill-Burton Hospital Construction Bill 652

CURRENT COMMENT

Penicillin Available Through Normal Commercial Channels 653

Experimental Transmission of Rheumatic Fever 653

Antepartum Penicillin Therapy..653

(Subject Index on next page)

MEDICINE AND THE WAR

The Army 654

Surplus Medical and Surgical Equipment for Civilian Use.....655

Wartime Graduate Medical Meetings 655

ORGANIZATION SECTION

Statements on the Hill-Burton Hospital Construction Bill.....656

Postwar Medical Service.....658

Washington Letter 661

Bureau of Information Sends Summary Sheets to State Societies.662

A. M. A.-N. B. C. Network Radio Program 662

Council on Medical Service and Public Relations 662

Woman's Auxiliary 662

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See also SAUNDERS Announcement—Pages 3, 4, 5

SUBJECT INDEX TO THIS ISSUE

The letters used to explain in which department the matter indexed appears are as follows: The Star (*) indicates an Original Article; "ab," abstract; "E," Editorial; "C," Correspondence; "MI," Medicolegal; "ME," Medical Economics; "OS," Organization Section.

A. M. A. Bureau of Information OS-658; OS-662
Col. Bickel as liaison officer OS-660
Committee on Postwar Medical Service meeting OS-658
Council on Medical Service regional conferences OS-662
representatives statements on Hill-Burton Bill E-652; OS-656
Abdomen surgery, curare in anesthesia to improve muscle relaxation *642
Acid, ascorbic, toxic effect of continued large doses? 683
Agranulocytosis, acute, fatal from thiouracil *646
Allergy, endocrine 669
Altitude, high, anoxia ab-677
high, hemoglobin affinity for oxygen ... ab-674
Aluminum hydroxide gel, neutralizes gastric acidity ab-677
Amphetamine sulfate in obesity ab-675
Anemia, refractory, proteolyzed liver in .. ab-679
Anesthesia, general, in shock ab-678
use curare in to improve muscle relaxation *642
Anti-Rh agglutinins *633
Arlington County Society of Virginia public relations meeting OS-662
Army Specialized Training Reserve Program, qualifying test 654
Arteriosclerosis, coronary, fatal in boy of ten ab-679
Arteritis, bilateral temporal, with complete loss of vision *647
Association News 682
Automobile driving for amputee patients. OS-662
Back, fibrositis ab-679
Bickel, R. D., liaison officer at A. M. A. .. OS-660
Billig exercises for dysmenorrhea 684
Blind, further assistance advocated OS-661
Blindness, total, in bilateral temporal arteritis *647
Blood, penicillin level *639
transfusion, hemolytic reactions due to Rh incompatibility *627
transfusion, infectious hepatitis after 683
Board Examinations 673
Board for Coordination of Malarial Studies E-650
Boilers, substances to inhibit corrosion in .. 683
Bombs, flying, casualties from ab-678
Book Notices 681
Books Received ..... **Adv. Page 49**
Carbon dioxide, inhale for cough in tuberculosis ab-678
Chilblain, honey treatment ab-680
Coccidioidomycosis, primary *624
Committee on Postwar Medical Service. OS-658
Coravol, to inhibit corrosion in boilers 683
Cornea, lesions after operations for trigeminal neuralgia ab-675
Correspondence 672
Corrodicide, to inhibit corrosion in boilers .. 683
Cough, inhale carbon dioxide for ab-678
Council on Foods and Nutrition 649
Council on Medical Service 662
Cowell, E. M., honored by President Roosevelt 668
Curare use in anesthesia *642
Davidson lecture established OS-662
Deaths 670
Diaphragm, lesions ab-674
Dysmenorrhea. Billig exercises for relief ... 684
Edema, high fluid intake ab-674
Editorials 650
Endocrine allergy 669
Erythroblastosis, fetal *633
Exercises, Billig, for dysmenorrhea 684
Fibrositis of back ab-679
Fluids, intake high in edema treatment .. ab-674
Flying bomb casualties ab-678
Foreign Letters 668
Gonorrhea treatment, penicillin orally *639
Government Services 667
Heart insufficiency, high fluid intake in edema ab-674
Hemoglobin, affinity for oxygen ab-674
Hemolysis, reactions due to Rh incompatibility *627
Hernia, diaphragmatic ab-674
Hill-Burton Hospital Construction Bill E-652; OS-656; OS-660
Honey in treatment of chilblain, ulcers and wounds ab-680
Hormones, allergy to 669
Horton-Magath-Brown syndrome *647
Hospitals, Hill-Burton Hospital Construction Bill E-652; OS-656; OS-660
surplus supplies, subcommittee report. OS-659
Hubbard, Ralph W., prisoner of war 654
Hyperthyroidism, thiouracil for C-673
thiouracil for, fatal agranulocytosis after . *646
Immunization, sensitivity to Rh factor *627
Industrial employment of blind urged OS-661
health service proposed, England 668
medical service to organized labor, improvement of *621
Insignia for medical personnel in combat .. 654
Intocostrin use in anesthesia *642
Jewish Medical Association, endocrine allergy 669
Johnson, Victor, statement on Hill-Burton Hospital Construction Bill .. E-652; OS-656
Lee, J. S. M., Chinese flight surgeon here ... 655
Leukocyte picture in malaria 684
Licensure, temporary, laws on OS-659
Liver diseases, diagnostic puncture in .. ab-680
infectious hepatitis after yellow fever vaccine 683
proteolyzed, in refractory anemias ab-679
Los Angeles, regional conferences OS-662
Lueth, H. C., progress report on questionnaires OS-658
Malaria, leukocyte picture in 684
treatment, coordinated research for testing drugs E-650
Marriages 669
Medical Education, opportunities for medical officers OS-659
questionnaires sent to medical officers. OS-658
refresher courses for medical officers 654
Wartime Graduate Medical Meetings 655
Medical Examinations and Licensure 673
Medical Service, improvement to labor *621
postwar, committee meeting, Feb. 10 .. OS-658
Medical Supplies, surplus for civilian use 655; OS-659
Medicine, epochs in *621
socialized, and labor *622
Medicine and the War 654
Meningitis, prevention, sulfadiazine for .. C-673
Meningococcemia, fulminating, penicillin for *645
Meningopneumonitis virus, penicillin treatment E-652
Mouth infections, penicillin pastilles for . ab-678
Muscle relaxation, curare in anesthesia to improve *642
National Neuropsychiatric Institute proposed OS-661
Nerves, vagus-sympathetic block ab-680
vagus-sympathetic block in shock ab-680
Neuralgia, trigeminal, corneal lesions after operations for ab-675
Neuropsychiatric Institute proposed, Washington, D. C. OS-661
News 663
Nurses, graduate (unmarried), house votes to draft OS-661
recruitment, organizing 655
Nystagmus, rotary 684
Obesity, amphetamine sulfate for ab-675
Organization Section 656
Otitis Media, chronic, penicillin orally *640
Oxygen, affinity of hemoglobin for ab-674
high altitude anoxia ab-677
Palestine, foreign letter from 669
Pediatrics, penicillin treatment in ab-676
primary coccidioidomycosis *624
Penicillin, antepartum therapy E-653
now available to all E-653
orally *639
pastilles in oral infections ab-678
treatment in pediatrics ab-676
treatment of fulminating meningococcemia. *645
treatment of scarlet fever 684
treatment of venereal disease OS-661
treatment of virus diseases E-652
will it be used indiscriminately? C-672
Physicians, Royal College of, report on proposed industrial health service 668
Placenta permeability, fetal erythroblastosis. *633
permeable to penicillin E-653
Pneumothorax, spontaneous ab-675
Poliomyelitis, anterior, in pregnancy ab-675
Portland, regional conference OS-662
Pregnancy, antepartum penicillin therapy .. E-653
poliomyelitis in ab-675
sensitivity to Rh factor *627
Prisoners, use for testing antimalarial drugs E-650
Psittacosis, penicillin treatment E-652
Purpura, fulminating meningococcemia *645
Queries and Minor Notes 683
Questionnaires sent to medical officers ... OS-658
Radio Broadcasts 682
Research, coordinated for testing of antimalarial drugs E-650
to be pressed after war OS-661
Residencies for returning medical officers. OS-659
Respiratory disease, sulfadiazine prophylactic ab-677
Rh factor, fetal erythroblastosis *633
hemolytic transfusion reactions *627
Rheumatic Fever, experimental transmission E-653
Royal College of Physicians report on proposed industrial health service 668
San Francisco regional conferences OS-662
Sanitation course for 25 hospital corps officers. 654
Scarlet Fever, treatment, penicillin 684
Self-medication danger with penicillin C-672
Sensenich, R. L., statement on Hill-Burton Hospital Construction Bill ... E-652; OS-656
Serum, etiology of infectious hepatitis 683
Shock, general anesthesia in ab-678
vagus-sympathetic block in ab-680
Societies, state, Bureau of Information sends summary sheets to OS-662
Sodium citrate buffer for oral use of penicillin *639
State Board Examinations 673
Stomach acidity, aluminum hydroxide gel neutralizes ab-677
Students, qualifying test for ASTRP 654
Sulfadiazine prevention of meningitis C-673
as respiratory disease preventive ab-677
Sulfanilamide plus penicillin in pediatrics. ab-676
Synovitis, multiple, complicating scarlet fever 684
Syphilis, penicillin orally for *640
Thiouracil, fatal agranulocytosis from *646
treatment of hyperthyroidism C-673
Thrombosis of temporal artery causing blindness *647
Tonics and Sedatives ..... **Adv. Page 36**
Tuberculosis, pulmonary, inhale carbon dioxide for cough in ab-678
Ulcers, honey treatment ab-680
Vaginitis, nonspecific, penicillin orally for .. *640
Venereal Disease, campaign planned to end by 1950 ..... OS-661
medical science eliminating OS-661
Veterans Administration, medical corps in. OS-660
Virus diseases, penicillin for E-652
Vital Statistics, death rate reduced 30%, Washington, D. C. OS-662
Vitamin C, little danger of harm from large doses 683
Washington Letter 681
Water supply system, inhibit corrosion in boilers 683
Waterhouse-Friderichsen syndrome, penicillin for *645
Woman's Auxiliary 682
World War II, ASTRP, announcement of qualifying test 654
care of inert patients during transit to base. 668
Chinese flight surgeons in U. S. 655
Committee on Postwar Medical Service .. 658
Cowell (E. M.) honored by Roosevelt 668
flying bomb casualties ab-678
Hubbard (R. W.) prisoner of war 654
medical officers and enlisted men repatriated 655
medical officers, refresher courses for 654
medical officers rescued on Luzon 655
medical personnel in combat, badge for 654
medical research to be pressed after war OS-661
nurses, house votes to draft OS-661
nurses, organizing recruitment 655
questionnaires sent to medical officers .. OS-658
sanitation courses for hospital corps officers 654
statement concerning discharges erroneous 654
surplus equipment for civilian use. 655; OS-659
treat Luzon internees 654
Wartime Graduate Medical Meetings 655
Wounds, honey treatment ab-680
Yellow Fever vaccine, infectious hepatitis after 683

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EPOCHS IN MEDICINE

THE IMPROVEMENT OF MEDICAL SERVICE TO LABOR

ERNEST E. IRONS, M.D.
CHICAGO

In the years previous to our present world war most of us were none too clear as to the changes in social and economic thinking that were insidiously creeping upon us. The stupendous war effort after Pearl Harbor, about which most of our daily activities now revolve, has still further diverted attention from the social and economic trends, which have been accelerated by the dislocations and modifications in living incident to the war. Some of these trends if properly guided will lead to salutary results for the nation; others if relegated to the hands of the ignorant may destroy the fruits of decades of effort. The real significance of still others is not immediately apparent without the aid of some perspective.

We can, however, get some notion of what the future has in store by looking back at the epochs of history, economic, social and medical. There we find almost exact parallels of many of our present problems, and from the experience of our forebears we can profit in the charting of our course.

Understanding of the epochs in medicine may be helpful in medical planning for our postwar period, especially with reference to the relations of medicine and labor.

The recent victories of medicine over disease in fields of infections and in surgery are deeply satisfying when compared in retrospect with what was possible in the prevention and cure of illnesses thirty years ago. Compared to the vast number of unsolved problems of disease, however, these victories are but local skirmishes in an age old battle and should serve only to stimulate and direct future effort. Nor are the problems of medicine limited to those of former years; there have been added those that have come as a result of alterations in the methods and weapons of war, and of the economic and social changes of peace.

Consecutive epochs of medicine cannot be clearly defined, but each shades into its successor as new knowledge has amplified and modified the conclusions drawn from previously known facts. The medicine of Hippocrates and Galen was a combination of limited observations and metaphysical reasoning, which allowed slow progress; it led to some sound and also to some queer conclusions and became stagnant under the domination of tradition and authority. The growth of anatomy, pathology and physiology in the seventeenth and eighteenth centuries slowly corrected false beliefs, and in the nineteenth century the beginnings of biochemistry and bacteriology made medicine more rational and scientific. On this foundation of centuries the marvelously rapid progress thus far in the twentieth century was achieved.

These epochs of medicine are inextricably interwoven with those of the political and economic history of nations and follow a similar pattern. The events of one period carry over and condition those of succeeding periods. The aggrandizement of the rich at the expense of the poor laid the foundations for the French Revolution, which in turn went far beyond a reasonable correction of ills, by destruction of property and loss of valuable lives. Many of the abuses remained uncorrected and contributed to the unstable social and political conditions during the Napoleonic wars.

In England in the eighteenth century the introduction of mechanical devices and use of water and steam power in manufacturing together with new methods of transportation led to the collection of people in larger groups in cities and created new economic and social problems in collective living and likewise, though largely unrecognized at the time, new medical problems. The increased incidence of rickets was the result of living indoors in crowded tenement areas with the smoke of industry obscuring such sunlight as was available.

Much the same kinds of factors became operative here in our own political, economic and medical evolution of the nineteenth century. With respect to the general public welfare, they have been at once curative and disease producing. The intense industrialization of cities of the twentieth century has made possible our amazingly successful war effort but at the same time has accentuated the economic and social ills from which we were already suffering. The acute congestion in new war plant areas with housing shortages and ill provided and shifting populations has been met by some temporary expedients, which are acceptable in the absence of better and safer measures but cannot continue after the war. Nor will they be necessary, because to a large extent these populations will have gone elsewhere.

There remains with us the medical problem of proper care of all the people, who stem from many races and nationalities, some of which are still incompletely assimilated. This problem is intimately connected with our economic and social life. Medical inadequacies in many regions are coincident with and often are directly traceable to economic deficiencies. The cure of the medical defect can be accomplished only by simultaneous improvement of social conditions. Medicine can and will do much to help but cannot do it all.

Under our present system of medical free enterprise the steady growth in efficiency of medicine in the prevention and cure of disease is continuing from year to year. In large cities and congested areas, slum clearance and improved housing need medical cooperation but are primarily economic and social problems. Many rural areas receive insufficient medical care. The

remedy will no doubt include new hospital and diagnostic centers to be established under local, county and state control and if necessary the voluntary location of qualified physicians on temporary or partial but adequate salaries paid by governmental and other agencies. The populations themselves in such areas will require education as to their own needs as well as to the availability of the new facilities. Better distribution of physicians to these poor, backward or sparsely populated areas will be practicable under any plan only when it is made possible for the doctor to live and raise his family in reasonable comfort, with some cultural advantages for his children.

Voluntary insurance plans, including those sponsored by local groups, medical societies, hospital associations and large insurance companies, are growing daily in numbers and coverage, so that millions of workers are given protection against the hazards of illness. These measures of social and medical care are developing in an orderly way at an ever increasing tempo, with the elimination of unsound features as experience accumulates.

There are now those who sometimes with sincere intent but often actuated by political motives would revolutionize medical practice and thereby destroy standards which have already demonstrated their worth in giving this country the highest quality of medical care in the world. In place of a sound and progressive program, the advocates of socialized medicine urge that there be substituted a system of government enforced provision for medical care supported by a tax of 1.5 per cent on payrolls of the employer and 1.5 per cent more of the first $3,000 deducted from the pay check of the worker, directed by a central bureau headed by the Surgeon General of the Public Health Service and served by doctors to be employed by the government and by hospitals selected by the government. This plan envisages the establishment of a bureaucracy far greater than any other in our government and presents also vast political possibilities. Such plans stifle initiative in the physician and at the same time reduce the level of quality of service for all. When such criticisms are made to advocates of government controlled medicine they reply that failure of their experiment, which involves the lives and welfare of one hundred million people and an annual expenditure of almost two billion dollars, is insignificant because they can then change it.

Says one of their spokesmen [1] "Distribution of medicine has always been faulty. The war has only brought it into sharp relief by the dislocation of populations, which has made it evident to us that our present system of distribution cannot be carried on. It has also shown us that local control is not satisfactory. The condition is particularly imminent at this moment and favorable to a change, because we shall also have to allocate and place in various parts of the country where they are most needed the medical officers who will return from the Army." And so they plan to ration by bureaucratic order the sixty thousand doctors on their return from fighting on foreign soil for the freedom of their homeland.

And "anyway," they say, "medicine must be entirely reorganized along new lines" and "cannot be left under the old patterns." This is the kind of unscientific and theoretical planning that a few vocal propagandists would impose on the American people and on the American doctor!

1. Should We Adopt Government Health Insurance? University of Chicago Round Table, number 354, National Broadcasting Company, Dec. 31, 1944, p. 3.

Audaciously they accuse physicians as being responsible for the glaring faults in their plans, saying that the doctors in general failed to cooperate with them in the formation of plans. Actually their whole program was conceived and delivered by a small group of armchair theorists including a few misguided doctors who had neither the experience in medical problems nor the appreciation of the patient-physician relationship which would entitle them to presume to speak for medicine or the public interest.

Socialized medicine will inevitably reduce standards of performance in diagnosis and treatment to a lower average level in the alleged effort to aid distressed areas. These areas should have relief, but it would be as reasonable to destroy part of a prosperous farmer's crop so as to lessen the discrepancy between him and his less fortunate or less industrious neighbor as to reduce standards of medical practice by measures which will not help but rather will ultimately accentuate the deficiency of medical care in depressed areas.

LABOR AND SOCIALIZED MEDICINE

The medical implications of socialized medicine, so clear to physicians who have stopped to think, are poorly understood by the majority of nonmedical people. Perhaps this is no more strange than the fact that relatively few people have attempted to think through the problems of permanent world peace such as come to the fore toward the close of each war. Currently over one hundred books and innumerable articles have been written about peace. In medicine remarkable progress has been made in methods of the cure of disease and in lessening the duration of individual illness. Life expectancy, especially in the industrial and lower income groups, increased from 34 years in 1879 to 64 years in 1942. These advances together with the increase in number of available hospitals from one thousand to seven thousand in thirty years now have made possible actuarially sound hospital insurance at a price which the man of limited means can afford. Even since the first hospitalization plans were inaugurated a lessening of need as expressed by duration of hospital stay has occurred. The average need of 5 hospital beds per thousand of population which prevailed in 1920 is now nearer 3.5 beds per thousand because of improvement in medical service. The utilization of this accomplishment awaits the education of the public and the formation of resultant favorable public opinion.

While it might appear that medicine has been slow to publicize its own progress, definite programs can be proposed with reasonable assurance of safety and soundness only when sound acturial statistics are available.

It is not surprising that organized labor, which represents a substantial portion of our population, has had difficulty in understanding the medical problem as applied to itself. This attitude of labor is understandable on review of its successes and its disappointments. The development of the labor movement, now over a hundred years old, has for its object the improvement of standards of living of the artisan and laborer. Such improvement is an important part of the desirable social changes and advances that have come in the complex of national and world living. Improved standards of living have come under the inspiration and guidance of many wise and forceful leaders. This extension has been delayed in certain periods and localities by the assumption of leadership by self-seeking reckless demagogues, whose actions have raised serious question as to their loyalty alike to their cause and to their coun-

try. At times leaders have been unable to control sections of their own membership, so that the announced policies and promises of responsible leaders have been betrayed, to the detriment of the just cause of labor. In its operating agreements with employers representing capital, there have been breaches of contract now by one, now by the other. But through it all labor has come to occupy a prominent and essential part of our national, social and economic life. Observers might well anticipate, however, that labor is no better informed on the relationships of medicine than are other sections of the American public, and such is the case.

In past years medicine has found difficulty in getting even a conference with responsible labor leaders, notwithstanding the unquestioned importance to labor of the medical questions requiring discussion. Approaches were often made through management, which no doubt at once initiated distrust by labor. Cogent questions of measures to prevent exposure of shop employees to contagious disease of their sick colleagues, and more recently the cooperation of labor in industrial preventive medicine, first urged by physicians with a view to the protection of labor, have required much explanation before labor could be convinced of the overall desirability to labor of the measures proposed. Too often also the quality of medical care afforded labor by management in the early days did not inspire trust in the good faith of employers.

More recently, conferences have been held with labor and management concerning problems of physical fitness for specific operations in industry. As soon as labor representatives were assured of the sincerity of medicine, their resistance to conferences decreased. This is most encouraging. The holding of future profitable conferences will result in more complete understanding. Medicine has no "ax to grind"; medicine knows no class in providing its art and skill to the care of the sick.

The attitude of labor to socialized medicine is thus explainable by lack of information and possibly also by the use of the word "social," which has too often been loosely interpreted as having the connotation of "something desirable that we haven't yet got." If in place of socialized medicine there was substituted "government controlled medicine" the whole picture would be less attractive.

Just as the present stature of labor has been built by years of effort and vision, and standards of living of its members, though often still unsatisfactory, infinitely improved over those of former years, so the present achievements of medicine have been attained through decades and centuries of patient work and study. Neither labor nor medicine will care to contemplate the destruction of cherished ideals and standards. The establishment of socialized medicine in this country would destroy standards of medical practice and quality of service to the public, of which labor constitutes a large part. One of the aims of labor is to increase the economic freedom of its members; will labor wish to compromise this freedom by agreeing to the imposition of governmental medical domination? Will its members wish to be regimented as to their medical care and to join the panel of a state paid doctor, whose initiative and sense of personal responsibility to his patient are blunted by years of routine and unprogressive service? Both medicine and labor will do well to remember the adage of Benjamin Franklin "They that give up essential liberty to obtain a little temporary safety deserve neither liberty nor safety."

Present proposals for socialized medicine will result in a lowered quality of medical care for the worker. More important to us all, including labor, this is but the first step of a far wider plan for the socialization of our government. As each step is taken, the similarity to what took place in National Socialist Germany becomes apparent. Under the guise of improvement of medical care of certain groups of people whose present provision is clearly inadequate, measures are proposed which will lower the general level of care, so that the average of all will become inadequate.

As reiterated by Herbert Morrison in his discussion of the problems of English labor, "It is often forgotten today, as it was during the English industrial revolution, that the combination of capital savings and investment, with labor, made possible rapid advances in standards of living of workers as well as owners. The misfortune lay in the lag between standards for the well-to-do and for the less prosperous." Today efforts must be centered on the improvement of care for those groups in which it is deficient rather than on the reduction of the standards of living, including medical care, already enjoyed by labor as a part of the commonwealth.

The establishment of a system which provides low grade medical care will have the same effect in reducing the amount of care of a better grade as has cheap money in driving sound money out of circulation in the monetary system. In commerce and in medicine, if standards of living are to be maintained, quality of output must also be maintained. Reduction of quality lowers standards of living.

Our medical as well as our social and governmental problems must be solved with reference to our traditional ideology and economics and not with reference to what has seemed desirable to other nations differently situated. Nevertheless it should be noted that sweeping governmental plans looking to the socialization of medicine in New Zealand were decisively repudiated by popular vote in recent months, as soon as the people became aware of their real implications.

One of the most serious effects of the taking over of the practice of medicine by government as provided under proposed legislation will be the loss of personal, local, county and state responsibility and the substitution of a central governmental bureau. Already innumerable Washington bureaus seem to have taken over even legislative functions in that they are said to write 90 per cent of the bills passed by Congress; then under broad permissive provisions they undertake the functions of the federal judiciary and prosecute citizens for violations of laws which they themselves originated. Federal subsidies, some of which are beneficial to the nation as a whole, are in other cases made the instrument by which the will of a bureau is imposed on states and local communities. This system forces the sale of states' rights to a federal bureau for the price of a government subsidy.

This system will accentuate rather than decrease existing social injustices and tend toward totalitarian government, which in Germany eventuated in the attempt to rule the world and is now engulfing her in disillusionment and misery.

For the successful conduct of any community, moderate central government is necessary to secure justice and fair balance between cooperating elements. But, as in old Rome, when for political purposes government becomes paternal and proposes increasingly to order the lives of citizens, individual moral fiber

weakens and the state eventually crumbles. The nation is like the child who does not grow strong when everything is done for him. The sense of personal responsibility is lost. Socialized medicine will inevitably remove the feeling of personal responsibility of the state physician for the welfare of his patient, and the quality of medical service to labor as well as to the rest of the people will deteriorate.

Especially important is the distinction between those responsibilities that can best be undertaken by the individual and those that are more efficiently performed as a community effort. Experience has shown that some functions of complex community life cannot be carried out successfully by the individual, such as the defense of police power of home against thieves and aggressors, the protection of the larger community against external aggression by military force and in medicine the establishment of sanitary safeguards within and beyond the community borders by health departments and the Public Health Service. Here there is involved the process of dealing with situations and populations *en masse*, with a view to prevention and not cure of disease, by scientific and practical measures the effective employment of which requires lifetime study and experience of specially trained men. When, however, illness overtakes the individual, his care, while based on experience in the treatment of his disease, becomes a problem which cannot be met by mass measures if the rights of the individual are to be respected. The most ardent advocate of socialized medicine, when he himself becomes ill, properly demands that he be treated as a man and not as one of the herd.

The success of medicine on full time in the army is urged by some as evidence of the success of regimentation in the practice of medicine. It is forgotten that the patients are a selected, originally healthy group of soldiers who also are themselves completely regimented. The average conditions of army practice, other than the use of the best technical methods of medicine, are entirely different from those met in civilian life.

The experienced doctors who entered military service on a purely voluntary basis did so because of a wish to do their part in the service of the nation in a grave emergency. Their accomplishments were possible because they had been schooled in an atmosphere of freedom. The success of their efforts is attributable to their training and not to the system of regimentation under which they now work. The wish of an overwhelming majority is to finish the job and return, free to practice and advance in knowledge as they did before.

Over the centuries a progressive centralization of effort and division of labor have increased the production of goods, raised standards of living and increased leisure, in which benefits labor in common with the rest of the public now participates. For medicine this has meant increased facilities for study and fruitful research, more effective care of patients, and a remarkable increase in life expectancy. This prolongation of life, by which thirty years have been added in the present epoch in the most productive period of life, contributes directly to the rising standards of living.

Until the war is completely won, our primary thought is prosecution of the war effort, which has been carried on so magnificently on battle and home fronts by all, including labor and medicine. The war has made necessary the institution of innumerable restraints, policies and sacrifices of freedom to which the American people, who, after all, are the government, will not willingly submit after the war. Much less is it fair or wise during a period when men's minds are temporarily and willingly attuned to a necessary measure of regulation, and when a large proportion of the physicians of the country are away in its service, to impose a new system of regimentation which will fail to accomplish the ends for which it is avowedly proposed and also will destroy the standards already reached.

In the epoch which we are about to enter, the advances and service to mankind of medicine will be conditioned by coincident far reaching economic and social changes. Wise and forward looking counsel will be needed to guide these changes by evolution rather than by revolution which leads to destruction.

Medicine has always been and is now motivated by the desire to be of service to the public. To achieve this ideal, medicine must be free.

122 South Michigan Avenue.

PRIMARY COCCIDIOIDOMYCOSIS

A POSSIBLE PEDIATRIC PROBLEM

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It is only during the past few years that a clear concept of the pathogenesis and clinical features of coccidioidomycosis has become apparent. Until 1936 to 1938, when Gifford [1] and Dickson [2] described "valley fever" as the primary or initial coccidioidal infection, this disease was considered only as the disseminated granulomatous form with an ultimate poor prognosis. Now, however, we know that the initial infection in many ways resembles primary tuberculosis, that complete clinical recovery occurs in most instances and that the granulomatous form is a dissemination following a breakdown of the primary stage.

Most of the recent reports have been concerned with young adults in the military service, such as we are presenting today. However, one of the earliest reports of primary coccidioidomycosis dealt with this disease as it occurred in a group of children. In 1939 Faber, Smith and Dickson [3] reported 24 cases in children under 15 years of age and mention that in a questionnaire 3 per cent of patients were under school age and 18 per cent were of school age. Furthermore, Gifford, Buss and Donds [4] found 26 per cent of their 104 patients with "San Joaquin fever" to be younger than 20 years of age. Recently Hess [5] of Chicago mentioned the occurrence of disseminated coccidioidomycosis in a man aged 29 who had resided in endemic areas repeatedly since the age of 11 years. He had gone during winter months to convalesce from sinusitis and bronchitis.

From the medical and roentgenologic services, Ashford General Hospital, West Virginia.

Read before the Section on Pediatrics at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

1. Gifford, M. A.: San Joaquin Fever, in Annual Report, Kern County Health Department for the Fiscal Year July 1, 1935 to June 30, 1936.

2. Dickson, E. C.: "Valley Fever" of the San Joaquin Valley and Fungus Coccidioides, California & West. Med. **47**: 151 (Sept.) 1937.

3. Faber, H. K.; Smith, C. E., and Dickson, E. C.: Acute Coccidioidomycosis with Erythema Nodosum in Children, J. Pediat. **15**: 163-171 (Aug.) 1939.

4. Gifford, M. A.; Buss, W. C., and Donds, R. J.: Data on Coccidioides Fungus Infection, Kern County, 1901-1936, in Annual Report, Kern County Department of Public Health for the Fiscal Year July 1, 1936 to June 30, 1937.

5. Hess, J. H.: Personal communication to the authors.

We are presenting this paper before the Section on Pediatrics because we believe that this disease has not received the attention it deserves from a pediatric standpoint. Pediatricians practicing in or near endemic areas of southern California, southern Arizona, southern Utah and western Texas unquestionably are more familiar with this disease than those of us practicing in other parts of the country. However, with modern rapid transportation facilities and increase in migration of populations the disease may be seen throughout the entire United States. Our problem is that of recognition of coccidioidomycosis, particularly in children returning from endemic areas in the Western states, where they have been sent to obtain the advantages of a dry climate in the treatment of respiratory diseases. It is significant that Faber and his group [3] found that recent arrival in an endemic region was a predisposing factor. Evidently, acquired immunity occurs in a large proportion of individuals who have lived in endemic areas over a long period.

Sensitization to the fungus occurs following inhalation of contaminated dust, producing symptoms and tissue changes paralleling the primary infection in tuberculosis.[3] Dickson [6] suggests that the primary infection may be in the pulmonary parenchyma like the foci of Ghon.

We should be familiar with what might arbitrarily be considered three phases of the primary form: The acute stage, subacute or chronic active stage and the arrested or healed stage. Each is characterized clinically by significant features, the first by acute respiratory disease frequently associated with erythema nodosum and/or erythema multiforme and arthritic symptoms occurring usually two to three weeks after the initial infection. The subacute or chronic active stage may be considered as that period following the disappearance of acute manifestations in which, however, there is evidence of activity as manifested by changing pulmonary lesions in chest roentgenograms. This period may last from weeks to months. The last stage is designated as any time following disappearance of active infection when clinically silent lesions are demonstrated radiographically.

Our patients were mainly seen either in the second or in the third stage, as they were observed several weeks or months after they contracted the initial acute infection while in an endemic area. Briefly, a few words should be mentioned relative to the acute manifestations.

THE ACUTE STAGE

The acute stage is called by Smith [7] the acute respiratory "influenza" or "pneumonic" form (rarely diagnosed in civilian practice). The incubation period varies from eight to twenty-one days. The onset may be abrupt or insidious. Thoracic pain, pleuritic in nature, frequently bilateral, is common, occurs early, is usually prolonged and is aggravated by cough. In Goldstein and McDonald's [8] group of cases it occurred in 88 per cent, and an initial diagnosis of pleurisy was not infrequent. Cough is frequent, occurring in approximately 88 per cent of the cases, and is usually productive of yellowish brown sputum; at times particles of dust or sand may be observed. The cough may last a few days, two or three weeks, or, as in some of our cases, over a period of several months. Hemoptysis may occur and is unrelated to the severity of the symptoms or the pathologic condition of the lungs. Chills and fever are frequent and usually last from two to four days. The temperature may range from slightly over normal to as high as 104 F. and may last for a few days or persist as a low grade fever for weeks. Many of the patients complained of sore throats at the onset, and pharyngitis and tonsillitis was a frequent initial diagnosis. Smith [7] describes a fine macular generalized rash within the first few days of the onset resembling measles, scarlet fever or drug eruption. One of our patients recalled a measles type of rash on the third day of his acute symptoms. Physical examination may reveal signs suggestive of acute bronchitis, pneumonic consolidation or pleurisy. Within eight to fourteen days erythema nodosum and/or erythema multiforme occurs in 5 to 20 per cent of the cases. At this time arthritis pains occur rather commonly in approximately 30 per cent [8] unaccompanied by joint swelling. The lumbar spine and lower extremities are most commonly involved. During this stage the blood frequently shows an eosinophilia. The total leukocyte count is not significant. The sedimentation rate is consistently elevated and may remain elevated after an apparent clinical recovery. The coccidioidin skin test is positive.

SUBACUTE OR CHRONIC ACTIVE STAGE

In the second group we are considering those patients who have active disease but either give no history of an acute attack or have recovered from the acute clinical manifestations mentioned heretofore. Some of our patients have been previously hospitalized elsewhere because of fatigue, loss of weight, chronic cough, chest pain and some because of low grade fever. In many a diagnosis of coccidioidomycosis was suspected on the basis of a history of residence in an endemic area. In others, initial diagnoses of bronchitis, pulmonary tuberculosis, bronchiectasis, atypical pneumonia, pleurisy and asthmas were considered.

Examination usually revealed evidence of weight loss and slight elevation of afternoon temperature. Examination of the thorax frequently revealed no abnormal findings, while, in others, evidence of pleural thickening, areas of impaired resonance and harsh breath sounds were found. Rales were conspicuously absent except in 1 patient who had a coexisting bronchiectasis and in another who had active pulmonary tuberculosis. Another patient had an asthmatic type of wheezing. A presumptive diagnosis was based on a history of residence in an endemic area, occasionally with previous acute upper respiratory episode, a positive coccidioidin skin test, elevated sedimentation rate and radiologic evidence of active pulmonary disease on serial x-ray examinations. In some patients the fungus was isolated from the sputum by culture and in 1 by guinea pig inoculation; in others it was not found. Repeated sputum specimens and gastric washings were examined for tubercle bacilli and none were found except in the 1 case with cavitation.

CHRONIC ARRESTED OR HEALED STAGE

In the third group we have considered a group of circumscribed nodular lesions as found on radiologic examination, with a history of residence in an endemic area, responding with a positive coccidioidin skin test. Most of these were found on routine examination and were asymptomatic as far as pulmonary disease was concerned. The sedimentation rate was normal. Cough usually was absent and there was no sputum. Gastric

6. Dickson, E. C.: Primary Coccidiodomycosis, Am. Rev. Tuberc. **38**: 722 (Dec.) 1938.
7. Smith, C. E.: Coccidioidomycosis, M. Clin. North America **27**: 791 (May) 1943.
8. Goldstein, D. M., and McDonald, J. B.: Primary Coccidioomycosis, J. A. M. A. **124**: 557 (Feb. 26) 1944.

washings were negative for both fungi and tubercle bacilli.

Smith [9] has demonstrated arrested pulmonary lesions, some calcified, mistaken for tuberculosis roentgenographically and at autopsy. We were further encouraged with respect to our interpretation of these lesions by the opportunity of seeing a solitary coccidioidomycosis nodule in the right lung and scattered miliary nodules in the left lung of a soldier on whom an autopsy was performed for accidental death, as shown in the accompanying illustration. Grossly, the lesions resembled tuberculosis and showed evidence of both healing and activity. The diagnosis was established by demonstration of the fungus in tissue sections.

DIAGNOSIS

In establishing a diagnosis of coccidioidomycosis, the following points in the history are of great significance:

1. Residence or visits in an endemic area.

2. An acute episode of respiratory disease, not infrequently followed in two or three weeks by erythema nodosum, erythema multiforme or both.

Large caseous lesion of coccidioidomycosis in the right lung. Accidental death; no pulmonary symptoms. Organism found in lesion.

During the primary infection there may be hilar adenopathy, patchy parenchymal infiltration or pleurisy with effusion. One or all three manifestations may occur. The primary radiologic findings may be consistent with a bronchopneumonia or an epituberculosis and may be difficult to differentiate from childhood tuberculosis. In adults a mottled apical infiltration may resemble an acute reinfection type tuberculosis or atypical pneumonia. More rapid resolution of the acute lesions is seen in coccidioidomycosis than in tuberculosis. Cavitation may occur within the first few weeks of the disease, and the majority of the cavities are thin walled.

After recovery from the acute stage, physical findings are usually absent. Chronic cough and chest pain are frequent complaints. There may be an evening temperature elevation. Hemoptysis is not common. Sputum is not abundant and has no characteristic appearance. Many late cases are asymptomatic, and residual lesions are found on routine radiographic examination of the chest, which may show linear fibrotic markings, thickened pleura, atypical parenchymal infiltrations or nodular lesions resembling solitary tuberculous lesions, or metastases. Hilar adenopathy may or may not be present. Smith [10] and Carter [11] have described nodular lesions in the primary and arrested stages.

Colburn [12] states that "permanent fibrotic residues are not conspicuous. Areas of exudation clear fairly rapidly (ten to twenty days) but infiltrates require thirty to ninety days and occasionally longer." We believe that prolonged radiographic observation may show the presence of nodular densities after all other radiographic evidence of the disease has cleared.

Sarcoidosis, the lymphomas and fungous infections, other than coccidioidomycosis, must be considered in a differential diagnosis (Carter [11] and Fawcitt [13]).

The following 3 cases illustrate the necessity of considering a fungous infection as an explanation for nodular pulmonary lesions, or cavities, as observed on roentgenograms:

Case 1.—A routine chest examination in December 1943 showed multiple nodular lung lesions in a soldier hospitalized for a radial nerve injury. No primary malignant focus could be discovered, and investigation disclosed that in October 1942 he suffered an attack of "bronchopneumonia" while at a desert training station. Review of films made during this attack revealed soft, rounded infiltrations in both lungs, corresponding exactly to the sites of the residual lesions noted by us fourteen months later. He had a strongly positive coccidioidin skin test. These lesions were still present on the film made March 20, 1944, seventeen months after the initial infection.

Case 2.—A soldier with a history of training in a desert area, whose chief complaints were cough and chest pain, and who on admission six months after initial exposure showed hilar adenopathy and nodular parenchymal infiltration, developed several nodular pulmonary lesions during a five months period of observation. The coccidioidin skin test was positive, and sputum cultures revealed coccidioides immitis.

Case 3.—A patient examined to determine the cause of chronic cough showed a thin walled cavity in the right upper lobe on a chest roentgenogram. He gave a history of being stationed in a desert area eleven months previously. The coccidioidin skin test was positive. Tubercle bacilli were recovered from the sputum, and Coccidioides immitis was found in another specimen. Inoculation of one specimen produced coccidioidal lesions in the retroperitoneal lymphatics of a guinea pig, with demonstrable ascospores. Radiographically no distinction could be drawn between a tuberculous and a coccidioidal cavity in this case.

A positive intradermal test with coccidioidin indicates an allergic reaction comparable to the positive tuberculin test, i. e. either present or past infection. Rapid change from an inactive to a positive reaction is an indication of activity. A positive test may persist for years. Positive diagnosis is established by isolation of Coccidioides immitis from the sputum, or gastric washings cultured on Sabouraud's medium and confirmed by guinea pig inoculation.

Smith [7] states that precipitin and complement fixation tests have proved useful. However, up to the present time difficulty in obtaining the antigen has prevented widespread use of these tests. In mild initial infection these tests are negative, and the more severe the infec-

9. Smith, C. E.: Parallelism of Coccidioidal and Tuberculous Infections, Radiology **38**: 644 (June) 1942.

10. Smith: Coccidioidomycosis,[7] Parallelism of Coccidioidal and Tuberculous Infections.[9]

11. Carter, R. A.: The Roentgen Diagnosis of Fungus Infections of the Lung, with Special Reference to Coccidioidomycosis, Radiology **38**: 649 (June) 1942.

12. Colburn, J. R.: Roentgenological Types of Pulmonary Lesions in Primary Coccidioidomycosis, Am. J. Roentgenol. **51**: 1 (Jan.) 1944.

13. Fawcitt, R.: The Roentgenological Recognition of Certain Bronchomycoses Involving Occupational Risks, Am. J. Roentgenol. **39**: 19 (Jan.) 1938.

tion the more likelihood of their being positive. Precipitins are usually present in primary infections but rarely demonstrable in the disseminated form. The complement fixation rises with the severity of the infection, and these tests therefore may be of value in following the course of an active infection.

PROGNOSIS

The prognosis is usually excellent, although convalescence may be prolonged over a period of weeks or months and residual lesions may remain indefinitely. Only time will tell as to whether or not residual nodules disappear entirely or undergo complete calcification. All but one of Goldstein's [8] 85 patients recovered, and almost all were sent to duty within a period of several weeks to a few months. All but 2 of our patients, 1 with coexisting pulmonary tuberculosis and another with bronchiectasis, returned to duty of a limited nature. When dissemination occurs there is less than a 50 per cent chance of recovery. Treatment is purely symptomatic.

COMMENT AND SUMMARY

The radiographic manifestations of coccidioidomycosis are variable, but the initial pulmonary infection commonly resembles childhood tuberculosis or bronchopneumonia. One of the more common manifestations of the chronic stage of the disease is the appearance of single or multiple nodular lesions in the lung which may readily be confused with nodular tuberculous lesions or metastases from primary malignancy. Careful study of these lesions radiographically with a magnifying lens will usually reveal serration of the edges. As Carter [11] has so aptly stated, "It is, perhaps, more important to acquire grounds for the suspicion of a fungous disease than to acquire skill in differentiation between them."

ABSTRACT OF DISCUSSION

MAJOR WILLIAM H. WOOD JR., M. C., A. U. S.: The cause of coccidioidomycosis is a fungus which grows in the desert as hyphae. These long filaments break up into sections, or chlamydospores. When the chlamydospore is inhaled by animals or man it changes into an endospore, which is the pathogenic form of the fungus. Certain rodents seem especially susceptible to Coccidioidomyces. The Army makes use of this fact by examining the lungs of rodents in desert regions prior to staging maneuvers in these areas. Our patients with coccidioidomycosis have been few. Most of them lived in the East or Midwest. They were sent to California, Arizona, New Mexico or Texas for training purposes. They are young men who have had x-ray examinations of their lungs routinely or because they had respiratory infections. They come to us with a tentative diagnosis of tuberculosis. To differentiate coccidioidomycosis from tuberculosis, the clinical story is important. Location and appearance of the x-ray shadow is also helpful. Typically that of tuberculosis is retrosuprahilar, while that due to coccidioidomycosis is in the middle or lower lung fields. Cavities, if present, due to this condition have thinner walls and are more cystlike than those due to tuberculosis. The coccidioidin skin test, comparable to the tuberculin, should be employed. The sputum and gastric washings should be examined for fungi. There is a precipitin test and a complement fixation test, said to be helpful, but we have not been able to do these tests in our laboratory. The former is said to be present early, and the latter present in high titer during the secondary or granulomatous, spreading form. Other conditions which must be considered in the differential diagnosis are lymphoma, sarcoid and metastatic or embolic foci in the lungs. In some cases the physician is unable to establish the diagnosis with certainty. We feel that all such patients should be treated as though they had tuberculosis.

HEMOLYTIC TRANSFUSION REACTIONS DUE TO RH INCOMPATIBILITY

MANIFESTATION OF SENSITIVITY TO THE RH FACTOR MANY YEARS AFTER IMMUNIZATION BY PREGNANCY

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Routine cross matching of donor's cells with recipient's serum for demonstration of acquired isoagglutinins is inadequate. Since the transfusion service of this institution was centralized in November 1943 and all reactions were subjected to complete investigation by the personnel of the blood bank, nearly 1,000 transfusions have been given without evidence of a single reaction due to intergroup incompatibility. However, during this period there have been observed in 3 female patients 5 hemolytic reactions, all of which were due to acquired sensitivity to the Rh factor. In each instance cross matching had been carried out by the test tube centrifuge method, first at room temperature and later at refrigerator and body temperatures, without detecting incompatibility. This inability to predict intragroup reactions is due to the fact that many times the acquired Rh antibody is not demonstrable by in vitro tests.

The transfusion reactions which occurred in this hospital during the seventeen years prior to the organization of the blood bank cannot be tabulated with any degree of accuracy. However, so far as is known, the only previously observed intragroup hemolytic reaction was that described by Kariher and Spindler [1] in connection with a study of hemolytic disease of the newborn.[2] In view of our recent experience, the apparent scarcity of such reactions during the prebank period indicates that many were probably overlooked.

The cases presented in this report clearly illustrate the great length of time that may elapse between the last sensitization to the Rh factor and a subsequent transfusion reaction. Levine [3] states that once an individual is sensitized by the Rh factor that sensitization is probably retained throughout life. In this report are presented cases of proved retention of sensitivity nearly eight and sixteen years respectively after the last immunization by pregnancy.

Transfusion reactions due to Rh incompatibility may be typical or they may be bizarre, and therefore minor reactions can easily go undetected. However, if the Rh negative patient who has this minor reaction is given another transfusion of Rh positive blood he may have a more violent reaction which could prove fatal. It is of the utmost importance therefore to investigate all reactions, minor or severe, so that the exact cause can be determined and a recurrence of the accident, perhaps in a more severe form, be prevented. The procedure now used in this hospital in investigating transfusion reactions is presented briefly. Since it is desirable that all Rh negative individuals be transfused with Rh nega-

From the Departments of Medicine and Obstetrics and Gynecology, the University of Rochester School of Medicine and Dentistry, and the Clinics of the Strong Memorial and Rochester Municipal Hospitals.

1. Kariher, D. H., and Spindler, H. A.: Erythroblastosis Fetalis and the Blood Factor Rh, Am. J. M. Sc. **205**: 369 (March) 1943.

2. The desirability of using the term "hemolytic disease of the newborn" rather than "erythroblastosis fetalis" has been discussed elsewhere (by Kariher and Spindler [1] and by Kariher, D. H.: Erythroblastosis Fetalis [Hemolytic Disease of the Newborn] Occurring in One of Twins, J. A. M. A. **122**: 943 [July 31] 1943).

3. Levine, P.: Mechanism of the Isoimmunization by the Rh Factor of Red Blood Cells, Arch. Path. **37**: 83 (Feb.) 1944.

tive blood, our bank has now been organized in such a manner that this ideal can be achieved. A workable plan for the prevention of those intragroup reactions due to Rh incompatibility is presented.

REPORT OF CASES

CASE 1.—*History.*—E. S.,[4] a white woman aged 40, married, tertipara, quadrigravida, was admitted to the Strong Memorial Hospital on Nov. 14, 1943. Her blood pressure was 120/80. Her red blood cell count was 3,570,000, her hemoglobin 10.8 Gm. per hundred cubic centimeters.

A radical mastectomy was performed November 15. Immediately after the operation a transfusion of 500 cc. of citrated, 1 day old whole blood (group A, Rh positive) was given before she had reacted from the ether anesthesia. Fifteen minutes after the transfusion was completed she had a mild shaking chill, but at no time did her temperature rise above 100 F. Ten hours after the chill she voided dark amber urine, which unfortunately was not tested for hemoglobin. She had a moderate oliguria, and her postoperative course was further marked by nausea, frequent emesis and lassitude, but she did not become jaundiced.

Nine days after transfusion, when she was seen by a medical consultant, her hemoglobin was 11.2 Gm. per hundred cubic centimeters, blood nonprotein nitrogen 160 mg. per hundred cubic centimeters, creatinine 9.2 mg. per hundred cubic centimeters. Her blood pressure had risen to 160/90 but her fundi were negative and the cardiovascular findings were within normal limits. By the following day, when the possibility of a hemolytic transfusion reaction was first suggested, the blood specimens collected from donor and patient prior to transfusion had already been discarded. Nevertheless the investigations to be outlined presently were begun. During the next two weeks the patient's blood chemistry and blood pressure became normal and she gained strength rapidly. Aside from a urinary infection due to Escherichia coli her course thereafter was uncomplicated.

As shown in the table, further inquiry revealed that in 1925 she had had a miscarriage. In 1926 her second pregnancy was complicated by preeclamptic toxemia. Because of elevation of blood pressure to 186/102, ankle edema, persistent headaches and albuminuria labor was induced at eight and one-half months, and a normal female child was delivered. Her preeclamptic symptoms then promptly subsided and her blood pressure was never again found to be elevated until November 1943, as already mentioned. In 1927 she gave birth to a second normal female child after an uncomplicated pregnancy. On Feb. 7, 1936, nine years after the last pregnancy, she gave birth to a third female child. This baby appeared normal at birth but on the second day pronounced jaundice developed; the child became progressively paler, and the liver and spleen became palpable. On February 20 the red blood cell count had fallen to 1,810,000, the hemoglobin to 6.0 Gm. per hundred cubic centimeters and a single nucleated red blood cell was seen in a careful search of the blood smear. On that day she was given 50 cc. of blood from her father, and on the following day 75 cc. of blood. After each of these transfusions she became more deeply jaundiced but less pale. On February 23 the icterus index was 60, red blood cell count 3,190,000, hemoglobin 8.5 Gm. per hundred cubic centimeters. Thereafter the child steadily improved and has since been normal.

The only other item of importance in the patient's past history is the report of an intravenous pyelogram of March 19, 1941 showing pyelectasis of the right kidney and constriction of the ureteropelvic junction. It is possible that previous renal damage was partly responsible for the azotemia which developed after the transfusion reaction.

Blood Studies.—After the question of transfusion reaction was raised, it was learned that the blood of the patient and her family had been studied shortly before her operation in a laboratory separate from the blood bank. In the table are shown the

Chronological Order of Pregnancies, Operations and Transfusions in Cases Presented

	Pregnancies					Transfusions					
									Reaction		Years Since
Case	No.	Date of Delivery	Duration	Status of Child	Blood Type of Child	No.	Date	Donor's Blood Type	Febrile	Hemolytic	Last Sensitization
1	1	1925	3 mos.	Spontaneous abortion	?						
Patient, A_1 M Rh—	2	1926	8½ mos.	Normal	A M Rh—						
	3	1927	Term	Normal	A M Rh+						
Husband, O MN Rh+	4	1936	Term	Hemolytic disease	A MN Rh+						
		1943	Operation			1	11/15/43	A_1 MN Rh+	?	+	7+
2	1	1921	Term	Normal; died in infancy	?						
Patient, A_1 MN Rh—	2	1922	Term	Stillborn; monstrosity	?						
Husband, A_1 M Rh+	3	1924	Term	Normal	A_2 MN Rh—						
	4	1928	Term	Hemolytic disease	?						
	5	1929	Term	Normal	A_1 MN Rh—						
	6	1934	Term	Normal	A_1 MN Rh—						
		1944	Operation			1	6/2/44	O N Rh+	+	+	16
3	1	1928	Term	Normal	A_1 MN Rh+						
	2	1929	7 mos.	Stillborn	?						
Patient, A_1 N Rh—	3	1930	Term	Normal	O MN Rh—						
	4	1931	Term	Normal	A_1 MN Rh+						
Husband, A_1 M Rh+	5	1933	Term	Normal	A_1 MN Rh—						
	6	1934	Term	Normal	A_1 MN Rh—						
	7	1938	3 mos.	Induced abortion	?						
						1	8/ 1/38	A_1 MN Rh+	+	?	
						2	9/ 5/38	A Rh ?	—	—	
						3	9/10/38	A_1 N Rh+	+	?	
						4	9/13/38	A Rh ?	—	—	
						5	9/16/38	A_1 N Rh—	—	—	
	8	1941	3 mos.	Induced abortion	?						
						6	3/17/41	A_1 M Rh+	+	?	?
						7	3/18/41	A_1 M Rh+	—	?	
						8	3/21/41	O MN Rh—	—	—	
						9	3/22/41	O MN Rh—	—	—	
		1944	Operation			10	2/26/44	A_2 MN Rh+	+	+	
						11	2/28/44	A_1 M Rh+	+	+	
						12	3/ 1/44	A_1 N Rh+	+	+	
						13	3/ 3/44	A_1 MN Rh—	—	—	
						14	3/ 4/44	A_1 M Rh—	—	—	
						15	3/ 6/44	A_1 MN Rh—	—	—	

4. Dr. John J. Morton gave the authors the privilege of studying this case. Dr. John S. Lawrence first pointed out the probability of a hemolytic reaction by the patient.

blood groups of the S. family and of the donor who later provided a fresh sample of blood for grouping. No anti-Rh agglutinins could be demonstrated in the patient's serum against Rh positive cells from 3 individuals when tested before transfusion, but twenty-four days after she received the Rh positive blood the anti-Rh titer had reached a maximum of 1 : 32,000.[5]

On Nov. 26, 1943, eleven days after transfusion, the patient's red blood cells were completely agglutinated by anti-M serum,

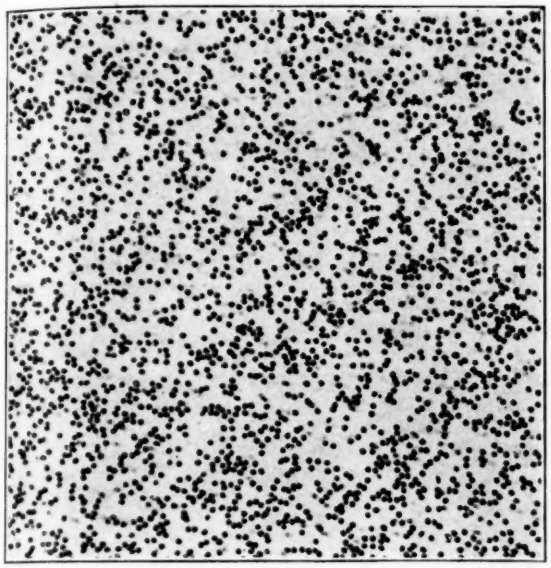

Fig. 1 (figures 1, 2, 3, 4 and 5 illustrate survival of transfused Rh negative cells, types M and MN, demonstrated by mixing anti-M serum with suspension of patient's cells [case 3, type N]) after transfusion with Rh positive blood, but before transfusion with Rh negative blood; no agglutination because all cells are type N (patient's).

but no agglutination occurred with anti-Rh or anti-N serums. Since the donor's blood was Rh positive, type MN, this test indicated that all of the transfused cells had been destroyed.[6] It is unfortunate that these studies were not carried out earlier, but even if a demonstrable portion of the donor's cells had survived to the tenth day this would have been only one-tenth the expected survival period for 1 day old citrated blood.[7]

CASE 2.—*History.*—E. P., a woman aged 43, quadripara, septigravida, was admitted to Rochester Municipal Hospital on May 31, 1944 for treatment of a relaxed pelvic floor with cystocele and rectocele. Her preoperative blood counts were red blood cells 4,000,000, hemoglobin 14.0 Gm. per hundred cubic centimeters, white blood cells 7,600. The urinary findings were normal. On June 2 a complete repair operation was carried out. In the course of the operation the patient bled profusely, so that supportive measures were indicated. Consequently, during and immediately after the operation the patient was given 700 cc. of isotonic solution of sodium chloride, 400 cc. of plasma and 500 cc. of group O blood to which 5 cc. of A and B specific substances had been added.[8]

There was no obvious immediate reaction (the patient was still under anesthesia) but in the evening of the day of operation her temperature had risen to 102 F. and the pulse rate was 182. Blood pressure was 90/65. The urinary output was only 50 cc. in the twenty-four hour period. By the following morning the temperature had risen to 103.4 F. and the patient was noticeably jaundiced. Her fluid intake this day was 2,800 cc. and her urinary output was 160 cc. By the third postoperative day (two days after operation) the icterus index was still 36 and the nonprotein nitrogen had risen to 92 mg. per hundred cubic centimeters. It was not until the twelfth postoperative day that these chemical findings returned to normal. Catheterized specimens of urine were negative except for a 2 plus reaction for albumin. Hemoglobin on the fourth postoperative day was 11.2 Gm. and red blood cells numbered 3,800,000. Two days later the hemoglobin had further decreased to 9.8 Gm. The patient gradually improved and made an uneventful recovery.

The patient's obstetric history as summarized in the table is of great interest. Following the transfusion the Rh status of the patient was investigated along with that of the available members of her family. These results are also shown in the table. Anti-Rh agglutinins were demonstrable in a low titer in the patient's serum three days following transfusion, whereas none were found in blood drawn prior to the transfusion. Five days following transfusion the anti-Rh agglutinin titer had risen to 1 : 32. Three days following transfusion complete destruction of the donor's cells, type O N Rh +, was easily demonstrated by tests with B, anti-M and anti-Rh serums, since the patient's type was A_1 MN Rh —.

CASE 3.—D. S., a white married woman aged 34, quintipara, octigravida, was admitted to the Rochester Municipal Hospital on Feb. 24, 1944. Two days later she underwent a complete repair operation which involved considerable loss of blood. During her first five postoperative days she received three whole blood transfusions of 500 cc. each, but nevertheless her hemoglobin remained at 8 Gm. per hundred cubic centimeters. On March 2, the day following the third transfusion, she was jaundiced, her icterus index was found to be 52, indirect bilirubin 8.7 mg. per hundred cubic centimeters, direct bilirubin 1.4 mg. per hundred cubic centimeters and hemoglobin was demonstrated spectroscopically in her serum. She had had none of the usual symptoms of a transfusion reaction, but her temperature had risen to 101 F. after the third transfusion.

Blood Studies.—Investigation revealed that the patient was Rh negative and all three donors were Rh positive, but anti-Rh agglutinins could not be demonstrated at any temperature in the serum drawn before operation or in any serums drawn during the next two months. Differential agglutination tests with anti-M and anti-Rh serums showed that on the day following

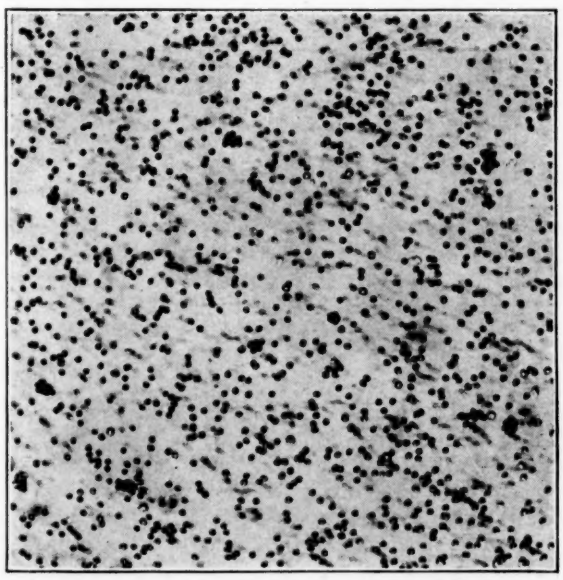

Fig. 2.—One day after first transfusion of Rh negative blood, type MN; an increasing degree of agglutination.

the second transfusion Rh positive (M and MN) cells were still present in the patient's circulation. Two days later, however, these cells and all of the third donor's cells had been destroyed. During the next four days she received three 500 cc. transfusions of Rh negative blood, which produced a rise in her hemoglobin to 13 Gm. per hundred cubic centimeters. Since the patient belonged to type N and the 3 Rh negative donors to types M or MN, it was possible to show an increasing percentage of cells

5. The results of the titrations of anti-Rh agglutinins were confirmed by Dr. Philip Levine. He agreed that this serum showed a definite prozone.

6. Wiener, A. S.: Hemolytic Transfusion Reactions: I. Diagnosis, with Special Reference to the Method of Differential Agglutination, Am. J. Clin. Path. **12**: 189 (April) 1942.

7. Wiener, A. S., and Schaefer, G.: Limitations in the Use of Preserved Blood for Transfusion, M. Clin. North America **24**: 705 (May) 1940.

8. Witebsky, E.; Klendshoj, N. C., and Swanson, P.: Preparation and Transfusion of Safe Universal Blood, J. A. M. A. **116**: 2654 (June 14) 1941. The A and B specific substances were supplied by the Eli Lilly Company, Indianapolis.

agglutinable with anti-M serum after each of the last three transfusions (fig. 1). Moreover, these Rh negative cells containing the M factor were still demonstrable in the patient's blood ninety days after the last transfusion.

The patient's previous transfusions and obstetric history are recorded in the table. From 1928 to 1941 she had had eight

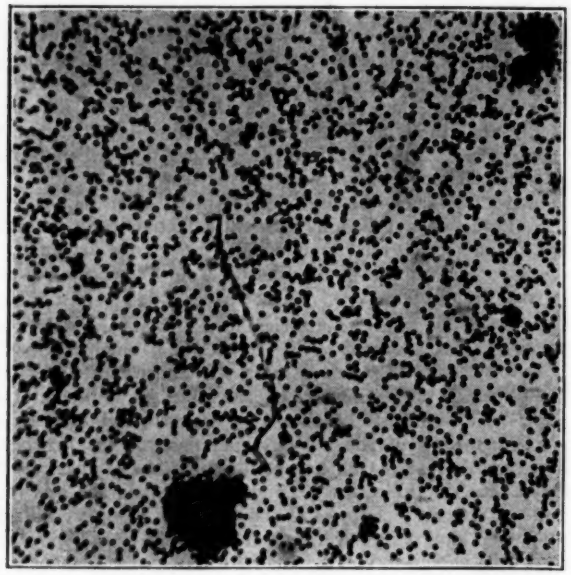

Fig. 3.—One day after second transfusion of Rh negative blood, type M; an increasing degree of agglutination.

pregnancies. Three of her 5 living children were found to be Rh negative and 2 Rh positive; the last Rh positive child was born in 1931. In 1929, after a pregnancy of seven months, she gave birth to a stillborn child with a meningoencephalocele. In 1938 and 1941 she had self-induced abortions after three months of pregnancy. The Rh type of the 3 fetuses is, of course, unknown. However, it is significant that at no time did she

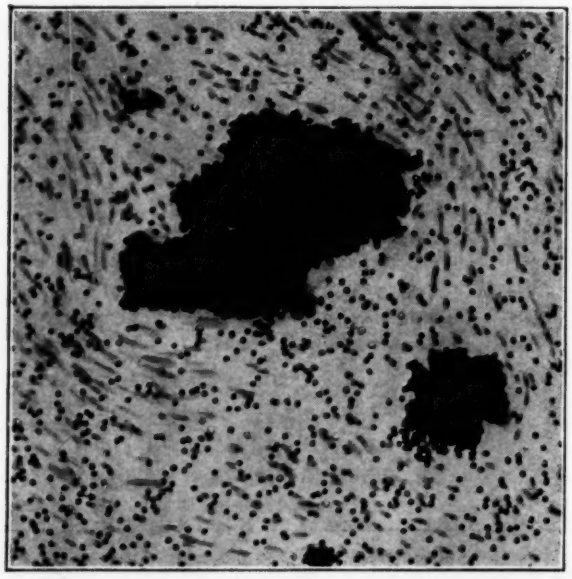

Fig. 4.—One day after third transfusion of Rh negative blood, type MN; an increasing degree of agglutination.

give birth to a child with manifestations of hemolytic disease of the newborn. Perhaps, if the last two pregnancies had been allowed to go to term, 1 or both of the infants might have suffered from the disease. Prior to the six transfusions described, she had had five transfusions after her abortion in 1938 and four more following the abortion in 1941. Although the patient's record gives no conclusive evidence of rapid destruction of the cells of these donors, it is noteworthy that she had chills and fever after three of the nine transfusions, and all 3 of these donors have been found to be Rh positive. On the other hand, the blood from the 3 individuals subsequently found to be Rh negative caused no reaction. Only once did she receive known Rh positive blood without recorded reaction. The Rh type of 2 of her previous donors has not been determined.

COMMENT

Clinical and Laboratory Diagnosis of Hemolytic Reactions.—It has been pointed out by Wiener and his associates [9] that in the majority of cases chills and fever following transfusion are due to nonspecific agents. On the other hand, the donor's cells may be destroyed rapidly because of specific incompatibility without causing any alarming symptoms. The mild chill of patient 1 was largely overlooked because she was under anesthesia and because it was not followed by any rise in temperature. In addition, her oliguria and passage of dark amber urine were disregarded and it was not until her blood nonprotein nitrogen was found to be 160 mg.

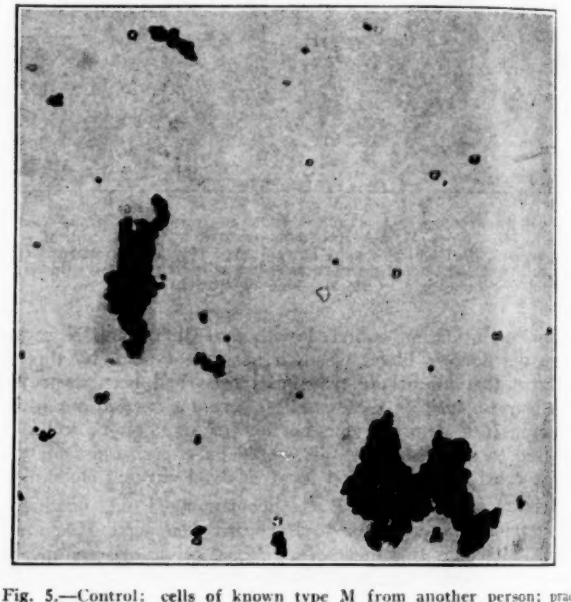

Fig. 5.—Control: cells of known type M from another person; practically complete agglutination.

per hundred cubic centimeters that a hemolytic transfusion reaction was suspected. In cases 2 and 3 the fever which followed transfusion was thought at first to be related to the operation, and the possibility of a hemolytic reaction was not considered until jaundice developed.

The importance of vigilance on the part of those in charge of transfusions and the necessity of systematic investigation of any untoward symptoms or signs cannot be overemphasized. The procedures to be followed in studying reactions have been set forth in detail by Wiener,[10] Schiff and Boyd,[11] Mollison [12] and others. In the Strong Memorial Hospital Mollison's plan is now adhered to as strictly as possible. This involves an attempt to demonstrate (1) the occurrence of increased blood destruction and (2) its cause. The

9. Wiener, A. S.; Oremland, B. H.; Hyman, M. A., and Sanwick, A. A.: Transfusion Reactions: Experiences with More Than Three Thousand Blood Transfusions, Am. J. Clin. Path. **11**: 102 (Feb.) 1941.
10. Wiener, A. S.: Blood Groups and Transfusion, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1943.
11. Schiff, F., and Boyd, W. C.: Blood Grouping Technic, New York, Interscience Publishers, Inc., 1942.
12. Mollison, P. L.: The Investigation of Hemolytic Transfusion Reactions, Brit. M. J. **1**: 529 (May 1), 559 (May 8) 1943.

form [13] shown in figure 6 has been found very convenient for recording essential data in chronological order. This form is filled out in duplicate with carbon paper. One copy is placed in the patient's chart and the other is kept in the files of the blood bank. The reverse side of the sheet is blank and is used for a description of the reaction and a statement regarding the conclusions reached by the investigation. The inadequacy of merely repeating the grouping and matching tests with the blood samples of donor and patient drawn prior to transfusion should be obvious from the experiences already cited.

Duration of Sensitivity to the Rh Factor.—It is now accepted that many hemolytic reactions occurring during pregnancy or the postpartum period are due to the development of Rh antibodies in Rh negative women who are carrying, or have recently given birth to, Rh positive children. However, the danger of transfusing such women with Rh positive blood many years later is not fully realized. In case 1 there was an interval of nearly eight years and in case 2 an interval of sixteen years between the birth of a child with hemolytic disease of the newborn and a hemolytic reaction following the first transfusion. In case 3 the Rh type of the last 2 fetuses is unknown. However, it is probable that at least one of them was Rh positive and therefore added to the immunization begun during the pregnancies of 1928 and 1931, so that the patient had a reaction after her first transfusion in 1938. It should be noted that Rh negative children were found in each of the three families presented in the table, thus indicating that each of the 3 fathers is heterozygous with respect to the Rh factor.

Since the Boston Blood Grouping Laboratory was organized in 1942, Diamond [14] has had an opportunity to examine the blood of 4 women in whom five years or more elapsed between the birth of the last child with hemolytic disease of the newborn and a transfusion reaction which revealed sensitization to the Rh factor. The oldest of these was a woman aged 54 whose last possible immunization by pregnancy occurred at least fourteen years before she had a hemolytic reaction following her first transfusion of Rh positive blood. Levine [3] has reported a case of probable hemolytic reaction in a woman following the first transfusion twenty-two years after the birth of a jaundiced child.

Wiener, Silverman and Aronson [15] reported the case of an Rh negative woman who had hemolytic reactions after each of three transfusions of Rh positive blood given eleven years after the birth of the last of 5 Rh positive children. In none of these children was there any evidence of hemolytic disease of the newborn; nevertheless the mother had been sensitized and retained her sensitivity for eleven years. Mollison [12] observed a similar case of hemolytic reaction in a woman fourteen years after the last of four presumably normal pregnancies. Vogel, Rosenthal and Levine [16] and Kouchy [17] demonstrated the presence of anti-Rh agglutinins in the serums of women following their first transfusions, which were given nine years and twenty-three years respectively after their last pregnancies. Neither of these women had had children suffering from hemolytic disease of the newborn. Determinations of the survival of the donor's cells were not made, but it is stated that no reactions followed these transfusions.

These observations and those reported in cases 1 and 2 support Levine's recent conjecture that immunization produced by the Rh factor probably persists for life.[3]

Limitations of In Vitro Tests for Rh Antibodies.—It has been found that anti-Rh agglutinins can be demonstrated in less than half of the Rh negative mothers of children with hemolytic disease of the newborn.[18] They usually disappear within six months to two years but have been found as late as six years after pregnancy.[19] Nevertheless, virtually all such mothers are presumably immunized against the Rh factor and may have and maintain tissue sensitivity when the antibodies cannot be detected in the test tube. The importance as regards transfusion reactions of antibodies bound to cells and not demonstrable in vitro has been amply discussed by Wiener [20] and Levine.[18]

STRONG MEMORIAL HOSPITAL - ROCHESTER MUNICIPAL HOSPITAL

INVESTIGATION OF TRANSFUSION REACTION

PATIENT'S NAME..... DIV..... UNIT NO.....

AGE..... SEX..... DIAGNOSIS.....

EXAMINATION OF BLOOD DRAWN FROM PATIENT AND DONOR BEFORE TRANSFUSION

DATE	BLOOD	GROUPING								GROUP	MATCHING				
		A SER	B SER	ABS B SER	A CELL	B CELL	ANTI Rh	ANTI M	ANTI N		DC + RS 0°	+ RS 20°	RS 37°	DS + RC 20°	RC + RS 0°
	PATIENT														
	DONOR														

EXAMINATION OF BLOOD DRAWN FROM PATIENT AFTER TRANSFUSION

	INTERVAL AFTER START OF TRANSFUSION	ANTI M	ANTI N	ANTI Rh	A SER	B SER	ABS B SER	
CELLS								
		HPN	HGB	II	BILIRUBIN		ANTI-Rh TITRE	
SERUM								

EXAMINATION OF BLOOD IN DONOR BOTTLE

CULTURE	
HEMOLYSIS	
LIPEMIA	

EXAMINATION OF PATIENT'S URINE AFTER REACTION

DATE	VOL.	COLOR	pH	UROBIL	HGB	MICRO

Fig. 6.—Form for recording in chronological order results of investigation of transfusion reactions. A SER, B SER and ABS B SER indicate A serum, B serum and absorbed B serum respectively used in grouping cells (and subgrouping A and AB cells). A cell and B cell indicate known A and B cells used in checking serums of recipient and donor for anti-A and anti-B agglutinins. Anti-Rh, anti-M and anti-N serums determine the presence or absence of these factors in cells of recipient and donor. DC = donor's cells; RS = recipient's serum; DS = donor's serum; RC = recipient's cells. RC + RS are tested at 0 C. as a check on cold agglutinins.

13. The rough mimeographed form shown in figure 6 will eventually be replaced by a printed form.

14. Diamond, L. K.: Personal communication to the authors in June 1944.

15. Wiener, A. S.; Silverman, I. J., and Aronson, W.: Hemolytic Transfusion Reactions: II. Prevention, with Special Reference to a New Biological Test, Am. J. Clin. Path. **12**: 241 (May) 1942.

16. Vogel, P.; Rosenthal, N., and Levine, P.: Hemolytic Reactions as a Result of Isoimmunization Following Repeated Transfusions of Homologous Blood, Am. J. Clin. Path. **13**: 1 (Jan.) 1943.

17. Kouchy, R. W.: Experiences with the Rh Substance in Transfusion Reactions, Minneapolis Med. **26**: 980 (Nov.) 1943.

18. Levine, P.: The Pathogenesis of Erythroblastosis Fetalis, J. Pediat **23**: 656 (Dec.) 1943. Potter, Davidsohn and Crunden.[19]

19. Potter, E. L.; Davidsohn, I., and Crunden, A. B.: The Importance of the Rh Blood Factor in Erythroblastosis, Am. J. Obst. & Gynec. **45**: 254 (Feb.) 1943.

20. Wiener, A. S.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group, Arch. Path. **32**: 227 (Aug.) 1941. Wiener.[19]

It is obvious that Rh incompatibility is a grave potential danger which must be faced by every one who has anything to do with the transfusion of whole blood or red cells. Although it has been sufficiently demonstrated that in the majority of instances this danger cannot be predicted by any sort of in vitro test thus far devised, Wiener's [15] biologic test is no doubt a more sensitive indicator of Rh incompatibility. Kouchy [17] states that Rh negative pregnant or puerperal women may be given Rh positive blood provided this test is negative. However, it seems entirely possible that in some cases of hemolytic reaction due to Rh incompatibility the hemolysis may be delayed beyond the test period of one or two hours and therefore may be missed. This might be expected particularly in patients whose last immunization by the Rh factor occurred many years prior to the transfusion. In such patients a number of hours or perhaps several days might be required for the anamnestic reaction [21] to manifest itself. The findings in case 3 illustrate this possibility. As previously pointed out, on the day after the second transfusion some Rh positive M and MN cells were still present in the patient's blood, but two days later these cells and all of the third donor's cells had been destroyed. This suggests an acceleration of the hemolytic process after each successive transfusion.

Another scheme advocated by Kouchy is that of completing the transfusion program within a period of five or six days before antibodies can develop. He suggests that Rh negative individuals may thus be transfused with Rh positive blood. Although this practice may result in few severe reactions, it should be pointed out that even the first Rh positive cells given to an Rh negative person of either sex may survive for a relatively short period in the patient's circulation.[22] The destruction of the donor's cells may not be sufficiently rapid to cause clinical symptoms and signs, but nevertheless the patient will be deprived of full benefit from the transfusion. A still more serious objection to Kouchy's proposal is that the injection of Rh positive blood into an Rh negative individual at any time may produce lifelong sensitivity to the Rh factor. This is particularly important in women who may thus lose their next child (or possibly their very first child) as the result of hemolytic disease, as suggested by Diamond.[23] Moreover, it should be emphasized again that Rh negative women, sensitized by pregnancy—even normal pregnancies many years before—may have severe hemolytic reactions following their first transfusion of Rh positive blood.

Plan for Prevention of Reactions.—In the light of our present knowledge it appears that the only safe plan for prevention of intragroup hemolytic reactions is that of giving only Rh negative blood to all Rh negative individuals. This practice is expensive and troublesome, but the recent experiences cited in this paper indicate that it is fully justified. The current policy of the Strong Memorial Hospital and Rochester Municipal Hospital is as follows:

1. Rh tests are performed free of charge on all donors, all transfused female patients, all obstetric and gynecologic patients and all male patients who have received more than two transfusions.[24]

2. When major surgery is contemplated for such patients, blood for grouping and Rh determination is sent to the bank before 8:45 a. m. of the day of operation. Except in emergencies, no female patient is sent to the operating room for major surgery unless her Rh type has been or is being determined.

3. Only Rh negative blood is given to the aforementioned Rh negative patients, and eventually this will be extended to include all males, regardless of their history of previous transfusions. Rh negative blood is also given to Rh positive infants with hemolytic disease of the newborn, as recently recommended.[25]

4. If Rh negative blood is not available in the bank when needed, it is purchased from professional donors, most of whom are members of the institutional personnel. This means that most of the blood purchased by the bank, with funds provided by private patients, is Rh negative.

5. A special effort is made to keep group O, Rh negative blood in the bank at all times. In emergencies, if it is necessary to give this blood to persons of group AB, A or B, 5 cc. of a solution of A and B specific substances is added to neutralize the anti-A and anti-B agglutinins.

6. A transfusion requisition form, similar to that recommended by Butler, Danforth and Scudder [26] and by Barton [27] gives information regarding the obstetric history of the patient and any previous transfusion reactions. This serves to keep both the intern and the personnel of the bank on the alert for situations in which Rh incompatibility is apt to be found.

7. As an added measure of safety for Rh negative patients and in certain other cases, triplicate mixtures of donor's cells and recipient's serum are checked by the test tube-centrifuge technic [28] after standing at 37 C., room and refrigerator temperatures for one hour.

SUMMARY

1. The occurrence of hemolytic transfusion reactions due to Rh incompatibility in 3 women emphasizes the following points:

(*a*) Serious hemolytic reactions may follow transfusion without causing chills, fever or other dramatic symptoms or signs.

(*b*) Sensitivity to the Rh factor, once it is acquired, may persist for many years, probably for life.

(*c*) Rh incompatability is often unpredictable by any sort of in vitro matching test.

2. Prevention of such reactions consists only in always giving Rh negative blood to Rh negative patients. This necessitates a complete reorganization of the blood bank so that Rh negative blood will always be available.

3. The study of reactions involves not only the rechecking of the groups and cross matchings but, in addition, the chemical examination of the blood and urine as well as the determination of the survival of the transfused red blood cells.

21. Kariher and Spindler.[3] Levine.[5]

22. Dacie, J. V., and Mollison, P. L.: Survival of Normal Erythrocytes After Transfusion to Patients with Familial Hemolytic Anemia, Lancet **1**: 550 (May 1) 1943. Wiener.[20]

23. Diamond, L. K.: Hemolytic Transfusion Reactions Due to the Rh Factor: A Preventable Danger, New England J. Med. **227**: 857 (Dec. 3) 1942.

24. The anti-Rh serums used in all determinations are of the 87 per cent variety. The various types of anti-Rh serums have recently been discussed by Levine.[3]

25. Wiener, A. S., and Wexler, I. B.: Transfusion Therapy of Acute Hemolytic Anemia of the Newborn, Am. J. Clin. Path. **13**: 393 (Aug.) 1943. Mollison, P. L.: The Survival of Transfused Erythrocytes in Hemolytic Disease of the Newborn, Arch. Dis. Childhood **18**: 161 (Dec.) 1943. Levine, Burnham, Katzin and Vogel.[28] Kariher and Spindler.[3]

26. Butler, B. C.; Danforth, D. N., and Scudder, J.: The Rh Factor in Intragroup Blood Transfusion Reactions, Surg., Gynec. & Obst. **78**: 610 (June) 1944.

27. Barton, F. E.: The Management of a Blood Bank at the Massachusetts Memorial Hospitals: The Problem of Rh Typing, New England J. Med. **230**: 749 (June 22) 1944.

28. Levine, P.; Burnham, L.; Katzin, E. M., and Vogel, P.: The Role of Isoimmunization in the Pathogenesis of Erythroblastosis Fetalis, Am. J. Obst. & Gynec. **42**: 925 (Dec.) 1941.

FETAL ERYTHROBLASTOSIS

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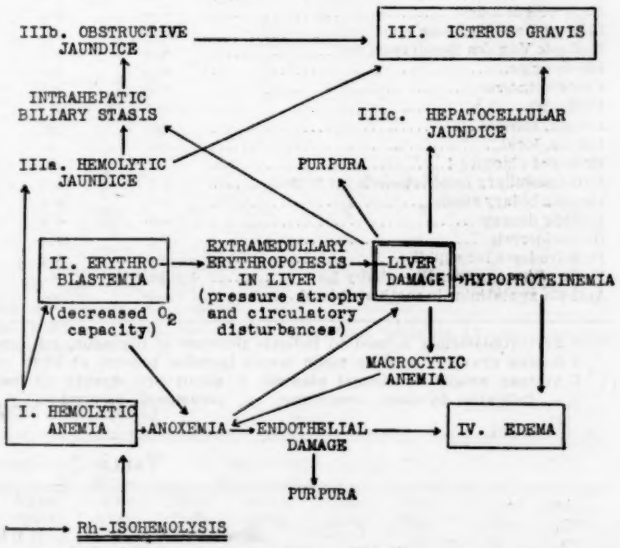
CHICAGO

The diagnosis of fetal erythroblastosis does not, as a rule, present serious difficulties to those familiar with its clinical picture and laboratory findings. However, in some instances the diagnosis is not easy. The difficulties are due to several reasons. One is that the term actually includes three distinct clinical entities: fetal hydrops, icterus gravis and congenital anemia of the newborn. The fact that they are related genetically and etiologically and that children of the same mothers may alternatingly manifest any one of the three forms of the disease does not lessen the diagnostic difficulties in individual cases. Another source of difficulty is that there are mild forms of the disease which may be overlooked or misinterpreted. The third difficulty is that none of the manifestations of the disease are pathognomonic. Every one of them may be found in certain other diseases.

The diagnostic difficulties have been thrown into sharp focus because the diagnosis of fetal erythroblastosis has assumed increased practical importance since the recognition of the role played by the Rh factor [1] has led to advances in therapy which permit the saving of many children that would have died in the pre-Rh era.

My main purpose in this paper is to show how the study of the Rh factor can be helpful in the diagnosis of fetal erythroblastosis, especially in cases with diagnostic difficulties. The Rh factor was studied in all patients and in their parents and repeated hematologic studies were done whenever it was possible. Table 1 lists diagnostic findings in fetal erythroblastosis and in a group of diseases which may have to be differentiated from fetal erythroblastosis. The items listed in the uppermost column occur with varying frequency and intensity in fetal erythroblastosis. Any one of them or any combination of them may be present or absent. Not one of them is absolutely pathognomonic for the disease except anti-Rh agglutinins, the presence of which in the mother suggests strongly fetal erythroblastosis in the baby. However, that too is not an absolute rule. I have found several instances in which anti-Rh agglutinins were found in the mothers but the babies were born normal. One such case in which the agglutinins persisted from a previous pregnancy will be the subject of a special report.[2] The absence of anti-Rh agglutinins in the mother does not exclude the disease in the child, even if the Rh factor is responsible for the disease. It should also be kept in mind that a certain proportion (about 10 per cent) of cases of fetal erythroblastosis are not caused by isoimmunization by the Rh factor. All other findings may be present in certain other diseases.

The fact that anti-Rh agglutinins in the mother are, as a rule, specific for fetal erythroblastosis in the child, that they are not found as responsible agents in any other disease, and that the combination Rh positive father and baby and Rh negative mother is found in about 90 per cent of cases of the disease has added a new criterion for the diagnosis of the disease to the three known previously: the clinical, the hematologic and the pathologic. The new diagnostic aids are tests for the Rh factor in the father, mother and child, and for anti-Rh agglutinins in the mother. It would hardly seem necessary to state that the finding in a family of the previously mentioned Rh factor combination does not, by itself, prove that an illness, for instance jaundice, edema or anemia in a newborn child, is fetal erythroblastosis. Yet a tendency has become manifest recently to diagnose the disease on flimsy evidence, sometimes on no more evidence than that the mother is Rh negative. The finding of the characteristic distribution of the Rh factor may be used as evidence in favor of erythroblastosis, since it is found in 90 per cent of the disease. However, it should not be used as final proof; otherwise it may lead to inclusion of cases which have nothing to do with erythroblastosis, with resulting confusion. No student of the subject will deny that there are instances of hemolytic anemia of the newborn or of severe jaundice or of hydrops which are not



Pathogenesis of fetal erythroblastosis. Principle: Rh positive husband of Rh negative woman transmits the Rh factor to the fetus. Rh antigenic substances pass from Rh positive fetus through placenta and produce in mother Rh antibodies. The latter pass from mother to fetus through placenta, act in the fetus as hemolytic agents and start the sequence of interlocking pathologic changes as presented in this chart.

erythroblastosis fetalis. Septic infections and prenatal and neonatal bronchopneumonia may be associated with severe hemolytic anemia and occasionally with jaundice. It is sometimes extremely difficult to diagnose the underlying infection clinically. Only a necropsy may reveal it. There are instances in which even necropsy findings may not be unequivocal, for instance in premature infants and in stillbirth, especially in the presence of advanced maceration. The diagnosis of erythroblastosis may be difficult also in mild abortive cases. In all such cases a study of the Rh factor in the parents and child and of anti-Rh agglutinins in the mother may be of considerable help in arriving at a correct interpretation.

A few instances which illustrate the role of tests for the Rh factor in obscure cases have been reported previously.[3]

From the Department of Pathology, Mount Sinai Hospital.
Aided by a grant from the Committee on Scientific Research of the American Medical Association.
Read before the Section on Pathology and Physiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Levine, P.; Katzin, E. M., and Burnham, L.: Isoimmunization in Pregnancy: Its Possible Bearing on the Etiology of Erythroblastosis Fetalis, J. A. M. A. **116:** 825-827 (March 1) 1941. For further bibliographic references see Davidsohn.[3]
2. Davidsohn, I., and Perlstein, M.: Relation of Anti-Rh Agglutinins to Fetal Erythroblastosis, to be published.
3. Davidsohn, I.: The Rh Factor, M. Clin. North America **28:** 232-253 (Jan.) 1944.

The occasional need of differentiating fetal erythroblastosis from congenital malformation of bile ducts is demonstrated in the following case:

CASE 11.—An infant aged 11 days, a patient of Dr. Philip Aries, was admitted with a story of progressive jaundice starting on the third day of life and of severe anemia. The infant was born at term, the delivery was normal and the weight at birth was 8 pounds 14 ounces (4,025 Gm.). There were two previous children, 11½ and 6 years old, both normal since birth.

A few days after birth it was noticed that the stools were acholic and contained no bile or urobilin. The urine contained bile but no urobilin. The icterus index in the blood serum was 150 and there was a prompt biphasic Van den Bergh reaction. The blood findings are recorded in table 2. Other laboratory findings were reticulocytes 9.4 per cent, platelets 188,000, coagulation time four minutes, bleeding time three minutes.

The acholic stools, the absence of urobilin in the feces and urine and the presence of bile in the urine prompted the diagnosis of obstructive jaundice probably due to congenital atresia of the bile ducts.

The anemia, erythroblastemia and jaundice suggested the possibility of fetal erythroblastosis. The mother was found to be Rh negative and her serum contained anti-Rh agglutinins. The baby, the father and the 2 older children were Rh positive.

An exploratory operation was decided on. The bile ducts were found patent. Within a few days following the exploratory operation bile appeared in the stool and urobilin in the urine; the jaundice began to decrease and soon disappeared completely. Bile in the urine decreased gradually and eventually disappeared. The response of the anemia to blood transfusions is shown in table 2.

There is no doubt that this was a case of erythroblastosis. It is possible that the biliary obstruction was due to a plug of thick inspissated bile, which is known to have a thick consistency in hemolytic jaundice. Probing of biliary passages by the surgeon may have dislodged the plug and brought about drainage.

Temporary acholia of stools in newborn infants with severe jaundice lasting for several days and weeks is known to occur and has been quoted in the literature as leading to the erroneous diagnosis of congenital obliteration of bile ducts. Three views have been advanced as explanations: As a result of excessive hemolysis the bile becomes too viscid to pass freely along the bile channels, the bile coagulates and forms bile thrombi and, thirdly, damaged liver cells overtaxed by excessive excretory work fail to function.

The case to be reported now illustrates a diagnostic problem of similar nature as in the preceding but where a study of the Rh factor did not help:

CASE 13.—A girl aged 4 days, a patient of Dr. B. M. Gasul, was admitted with a history of jaundice since birth, two blood counts showing 2,800,000 and 3,000,000 red cells and 55 and 60 per cent hemoglobin. The mother had one previous miscarriage. The child was A Rh positive and was given 165 cc. of A Rh negative blood, following which her red count went

TABLE 1.—*Differential Diagnosis in Live Born Infants*

	Fetal Erythroblastosis	Congenital Syphilis	Antenatal Infection	Postnatal Infection	Hemorrhagic Disease of Newborn	Congenital Malformation of Bile Ducts	Congenital Malformation of Heart	Icterus Neonatorum
Familial incidence	++	++	—	—	—	—	—	—
Splenomegaly	++	++	+	—	—	++	+	—
Hepatomegaly	++	++	—	—	—	++	+	—
Anemia	++	++	++	—	±	—	—	—
Leukocytosis	++	++	++	+	—	—	—	—
Leukemoid blood picture	++	++	++	+	—	—	—	—
Erythroblastemia *	++	++	+	—	—	—	+	—
Icterus gravis †	++	++	++	—	—	++	—	—
High icterus index	++	++	±	—	—	++	—	+
Indirect Van den Bergh reaction	++	++	+	—	—	—	—	+
Biphasic Van den Bergh reaction	++	++	+	—	—	++	—	—
Bile in urine	++	++	+	—	—	++	—	—
Urobilin in urine	++	++	++	++	++	—	++	++
Purpura	++	++	++	—	++	++	—	—
Edema, general	±	±	—	—	—	—	—	—
Edema, local	+	+	—	—	—	—	—	—
Enlarged placenta ‡	+	++	—	—	—	—	—	—
Extramedullary hematopoiesis (at term)	++	++	+	—	—	—	+	—
Hepatic biliary stasis	++	++	+	—	—	+	—	—
Hepatic damage	++	++	+	—	—	+	—	—
Hemosiderosis	++	++	±	—	—	—	—	—
Positive tests for syphilis	—	++	—	—	—	—	—	—
Father Rh+, mother Rh—, baby Rh+	++ in 90%	—	—	—	—	—	—	—
Anti-Rh agglutinins in mother's blood	++	—	—	—	—	—	—	—

* Erythroblastemia is used to indicate presence of immature nucleated red blood cells in circulation in excess of 1,000 per cubic millimeter.
† Icterus gravis is used to mean severe jaundice present at birth or within 48 hours after birth and lasting beyond the first week of life.
‡ Average weight of normal placenta is about one seventh of body weight.
++ indicates frequent occurrence; +, occasional occurrence; ±, uncommon occurrence; — indicates absence as a rule.

TABLE 2.—*Observations in Case 11*

Date	Red Blood Cells	Hemoglobin, Gm.	Color Index	White Blood Cells	Myelocytes	Segmented Neutrophilic Leukocytes	Lymphocytes	Monocytes	Normoblasts
10/22 (11th day of life)..	1,500,000	6.6	1.3	30,500	7	44	42	7	5,490
10/22 Blood transfusion, 200 cc. father's blood, A Rh— positive									
10/24	7,200,000	22	0.9	6,800	3	57	36	4	340
10/26 Blood transfusion, 150 cc. father's blood									
10/27	4,800,000	18	1.0	13,700	..	56	40	4	822
10/28	4,700,000	17	1.0	22,500					

up to 5,000,000, the hemoglobin to 23 Gm. The color index was 1.3, white blood cell count 22,000, stab cells 2 per cent, segmented leukocytes 78, eosinophils 2, basophils 1; nucleated red blood cells were present: 230 per cubic millimeter on the seventh day and 600 on the twelfth, none later. The red count remained normal without further transfusions, hemoglobin decreased gradually to 18 Gm., the white blood cell count to 14,000. The differential count showed a gradual decrease of segmented granulocytes: 61, 49, 46, 32 and eventually 29 per cent at the age of 20 days, with a corresponding rise in percentage of lymphocytes, thus assuming the normal pattern. A few days after birth it was noticed that the stools became acholic and showed no bile and no urobilin until the twenty-seventh day of life, when doubtful traces began to appear. The urine showed bile pigment. Urobilin was present during the first two weeks of life, then absent, to reappear again in the fourth week. The icterus index on the twelfth day of life was 160, with a biphasic Van den Bergh reaction. It was 110 on the seventeenth day, 43 on the twenty-seventh, the Van den Bergh remaining biphasic. On the day of discharge at the age of 38 days the icterus index was 21.

The clinical diagnosis was fetal erythroblastosis or congenital anomaly of the bile ducts. The father was A Rh positive, the baby A Rh positive, the mother O Rh positive, without anti-Rh or any other irregular agglutinins. In spite of this negative serologic finding the diagnosis of fetal erythroblastosis was maintained and the child not operated on. It improved gradually, the jaundice disappeared and the stools became normal. At the time of writing, the child is 6 months old and perfectly normal.

The severe jaundice and the anemia at birth favor the diagnosis of erythroblastosis of the type in which the Rh factor is not involved.

One of the important consequences of the discovery of the Rh factor has been its practical application to the treatment of fetal erythroblastosis. There seems little doubt that transfusion of Rh negative blood administered early and continued according to clinical indications constitutes an important improvement in the treatment of the disease. In the following case reports the beneficial effect of transfusions is emphasized by the circumstance that the anemia in the surviving child was much more severe than in the one that died.

TABLE 3.—*Observations in Case 3b*

Day	Transfusion	Red Blood Cells	Hemoglobin, Gm.	Color Index	Normoblasts in Cu. Mm.	White Blood Cells	Segmented Neutrophilic: Myelocytes, %	Segmented Neutrophilic: Metamyelocytes, %	Segmented Neutrophilic: Stab Cells, %	Segmented Neutrophilic: Leukocytes, %	Segmented Neutrophilic: Eosinophils, %	Basophils, %	Lymphocytes, %	Monocytes, %
Birth	.....	1,600,000	7.5	1.4	376,750	171,000	4	4	5	33	3	1	42	8
5 hrs.	65 cc. ORh—													
5½ hrs.	.....	3,690,000	11.6	0.9	122,700	10,000	5	..	5	44	1	1	42	2
13 hrs.	65 cc. ORh—													
22 hrs.	100 cc. ORh—													
2	.....	5,000,000	18.0	1.1	25,830	30,000	3	1	7	65	1	..	19	4
	70 cc. ORh—													
3	.....	4,790,000	18.6	1.1	15,932	12,000	1	1	1	61	3	..	25	8
4	.....	4,530,000	15.6	1.0	9,280	13,000	1	5	3	50	3	1	30	7
14	.....	3,740,000	10.6	0.8	.....	8,000	..	3	3	57	..	..	30	5
21	.....	3,590,000	10.4	0.9	123	12,000	..	5	1	44	1	..	47	4
25	.....	2,150,000	8.7	1.2	.....	15,000	..	3	1	42	2	..	44	8
26	100 cc. ORh—													
29	75 cc. BRh+	2,760,000	7.4	0.8										
30	20 cc. BRh+													
31	20 cc. BRh+													
32	.....	2,600,000	8.6	1.0	.....	15,000	..	..	4	42	4	1	37	12
	20 cc. BRh+													
40	.....	2,900,000	9.3	0.9	.....	12,000	1	..	2	30	1	..	57	9
53	.....	3,340,000	11.6	1.0	.....	15,000	1	2	3	38	2	..	48	6
69	.....	3,810,000	11.6	0.9	.....	9,000	..	2	7	32	2	1	54	1

At birth: icterus index 30; Van den Bergh biphasic; indirect Van den Bergh 3.7 mg.; total serum protein 4.4 Gm.; albumin 1.7 Gm.; globulin 2.7 Gm.; albumin-globulin ratio 1:1.6 Fourth day: icterus index 167; serum protein 5.6 Gm.

TABLE 4.—*Observations in Case 15*

Day	Transfusions	Red Blood Cells	Hemoglobin, Gm.	Color Index	Normoblasts per Cu. Mm.	White Blood Cells	Segmented Neutrophilic: Myelocytes, %	Segmented Neutrophilic: Metamyelocytes, %	Segmented Neutrophilic: Stab Cells, %	Segmented Neutrophilic: Leukocytes, %	Segmented Neutrophilic: Eosinophils, %	Basophils, %	Lymphocytes, %	Monocytes, %
4	.....	1,900,000	9.0	1.4	1,368	15,200	2	5	6	42	3	1	39	3
5	75 cc. A Rh—													
6	.....	3,200,000	12.0	1.1	372	12,400	3	9	3	49	4	..	28	4
8	.....	3,000,000	9.6	0.9	...	15,900	3	..	3	51	3	..	35	3
	100 cc. A Rh—													
9	.....	3,100,000	12.6	1.0	...	13,400	2	1	2	55	3	..	33	4
	100 cc. A Rh—													
14	.....	3,300,000	13.0	1.1	...	18,600	1	2	1	49	3	2	37	5
18	.....	3,300,000	9.0	0.8	...	10,400	1	..	3	36	2	..	50	8

Urine: Fourth day, bile +; 5th day, bile +, urobilin and urobilinogen + in dilution 1:10; 14th day, platelets 238,000.

CASE 3a (patient of Dr. M. L. Dale).—The first child was normal and 2 years old when the second child was born. During pregnancy a transient anemia (red blood cell count 2,900,000 and hemoglobin of 65 per cent) were found on one occasion. The delivery was normal. The child became jaundiced on the second day of life. One hundred cc. of blood of group O, the Rh factor of which was not determined, was given but only a short while before death. Blood findings on the third day of life are recorded in table 7. Blood platelets were 190,000 on two occasions. Fragility of the red blood cells was normal. The child died on the fourth day of life. The necropsy findings are given in table 8.

Case 3b.—The third child of the same family was born twenty-one months after the second. Pregnancy and delivery were normal. Birth weight was 8 pounds 4 ounces (3,742 Gm.). In view of the previous history of erythroblastosis, an Rh negative donor was available at birth (the hematologic data are given in table 3). The baby was B Rh positive, the father O Rh positive, the mother B Rh negative. The mother was examined repeatedly during pregnancy but did not show anti-Rh agglutinins, and none were found on repeated examinations after the birth of the child. Jaundice became manifest ten hours after birth but was probably already present at birth because the placenta was yellow. There was general edema involving the face, arms, abdomen, scrotum and legs. In addition to blood transfusions, treatment included 5 per cent glucose intravenously, calcium gluconate and vitamin K. The child was kept in an oxygen tent until nucleated red blood cells disappeared from the blood. The weight on discharge was 11 pounds 2 ounces (5,046 Gm.). The laboratory data are given in table 3. The low total protein and the reversal of the albumin-globulin ratio are of interest.

The anemia was much more severe than that of the child that died. In addition there was general edema, which usually makes for a bad prognosis. The child was given 300 cc. of Rh negative blood during the first forty-eight hours, 230 cc. of it during the first twenty-two hours. Rh positive blood was not given until the twenty-ninth day of life. The child which died received probably Rh positive blood and only a short time before death.

The following is another instance of prompt response to transfusions of Rh negative blood:

Case 15 (patient of Dr. Philip Aries).—The first child, aged 3½ years, was normal. The second child became jaundiced soon after birth. The spleen was slightly palpable; the liver was not palpable. The father was A Rh positive, the mother A Rh positive, with severe anemia and excellent response to blood transfusions (table 4).

That fetal erythroblastosis may occur without anemia and erythroblastemia is demonstrated in case 7 (patient of Dr. B. E. Sayre).

The first child was O Rh positive, 18 months old and was normal. In the present, the second, child jaundice was noted at the end of the first day. Pregnancy and delivery were normal. The father was O Rh positive, the mother O Rh negative, with anti-Rh agglutinins, the baby O Rh positive. The child was taken off the breast at the end of the first day. The liver and spleen were palpably enlarged. The temperature was 104 F. The child appeared lethargic, the face edematous. There was no pronounced anemia at any time. It is possible that anemia was averted by the transfusions of Rh negative blood. The jaundice decreased gradually. The fever subsided at the end of a week. Vaginal bleeding was noted on the fifth day, lasting two days. The patient was discharged after nineteen days, with the jaundice almost gone but irritability noted. The laboratory data and transfusion record are given in table 5. The child was readmitted at the age of 6 months. She had not been normal since she left the hospital. She was unable to hold her head erect. There were opisthotonos, a fever of 106 F., twitching, then coma. Lumbar puncture showed normal spinal fluid. Death occurred twenty-four hours after admission, from bronchopneumonia. The necropsy findings are given in table 8. At necropsy the liver showed no gross or microscopic abnormalities. The spleen, which was not enlarged, showed hemosiderosis. The absence of microscopic histologic changes in the liver is interesting. It is possible that at birth the histologic structure of the liver was similar to that seen in the other cases of the disease, in all of whom characteristic

Table 5.—*Observations in Case 7*

Day	Transfusion	Red Blood Cells	Hemoglobin, Gm.	Color Index	Normoblasts in Cu. Mm.	White Blood Cells	Metamyelocytes, %	Stab Cells, %	Segmented Neutrophilic Leukocytes, %	Eosinophils, %	Basophils, %	Lymphocytes, %	Monocytes, %
3	.....	4,100,000	16.0	1.1	313	31,300	..	4	72	1	..	15	8
4	.....	3,800,000	12.4	1.0	582	29,100	1	3	59	2	..	23	12
	100 cc. ORh—, mother's washed red cells in saline												
5	.....	4,900,000	9.4	0.7	...	27,500	..	..	60	1	..	24	15
	100 cc. ORh—, mother's washed red cells												
6	100 cc. ORh—												
7	.....	5,000,000	12.6	1.0	...	.....	..	..	77	4	..	12	7
	60 cc. ORh—												
8	.....	5,300,000	18.2	1.0	...	33,400	..	..	80	2	..	8	10
11	.....	6,100,000	19.7	1.0	...	26,400	..	3	52	6	..	27	12
17	.....	5,000,000	15.0	0.9	...	16,000	2	5	49	3	..	36	5
101	.....	5,000,000	17.0	...	...	22,000	..	..	16	10	1	65	8
6 mo.	.....	5,000,000	16.2	9.0	...	21,000	..	..	46	..	1	48	5

Table 6.—*Observations in Cases 8, 9 and 10*

Day	Transfusions	Red Blood Cells	Hemoglobin, Gm.	Color Index	Normoblasts per Cu. Mm.	White Blood Cells	Myelocytes, %	Metamyelocytes, %	Stab Cells, %	Segmented Neutrophilic Leukocytes, %	Eosinophils, %	Basophils, %	Lymphocytes, %	Monocytes, %
						Case No. 8								
4	.....	2,700,000	6.6	0.8	708	17,700	8	6	34	40	..	..	2	..
						Case No. 9 (Twin No. 1)								
2	.....	3,600,000	12.8	1.0	856	21,400	..	..	2	60	1	1	19	8
3	65 cc. O Rh—	3,400,000	11.4	1.0	264	4,400	..	..	..	40	..	..	..	..
4	50 cc. O Rh—						..	..	..	40	..	..	50	1
						Case No. 10 (Twin No. 2)								
2	.....	4,300,000	15.0	1.0	2,600	13,000	..	..	..	59	..	..	34	7
3	.....	3,700,000	14.4	1.1	206	10,300	..	..	..	30	..	..	64	6
	65 cc. O Rh—													
5	50 cc. O Rh—													

changes were found as recorded in table 8. Purpura was the cause of death in 3 children of the same family, 2 of them twins.

CASE 8 (patient of Dr. A. H. Levine).—The first pregnancy terminated in abortion in the third month. The second pregnancy and delivery of a boy were normal. Jaundice was noted on the third day, followed by listlessness, twitchings and rapid decline and death on the fourth day. The platelet count was 180,000, the coagulation time four minutes, the bleeding time two minutes. Other hematologic data are given in table 6 and the necropsy findings in table 8.

CASES 9 and 10.—Twins were born to the mother of patient 8 about fourteen months later, after a normal pregnancy and uneventful delivery. Jaundice was noted soon after delivery. There was no response to blood transfusions. The father was of Rh positive, but the latter was given only to babies 11 days old or older. The surviving babies received together 1,810 cc. of blood. The beneficial effect of transfusions and especially of Rh negative blood when administered early is evident.

Necropsies were done on 8 babies with erythroblastosis (table 8). Two had congenital hydrops, 1 a premature stillborn weighing 970 Gm., the other stillborn at term, weighing 2,800 Gm. They were the only 2 in the series without jaundice, although the larger showed biliary stasis in the liver. Jaundice may have been obscured by edema. Three were 3 days old, 2 were 4 days old and 1 was 6 months old at death. There was a history of familial incidence in 5 of them. Two

TABLE 7.—*First Blood Counts in Eleven Infants with Fetal Erythroblastosis*

No.	Age	Red Blood Cells	Hemoglobin, Km.	Color Index	White Blood Cells	Normoblasts per Cu. Mm.	Segmented Neutrophilic Myelocytes, %	Segmented Neutrophilic Metamyelocytes, %	Segmented Neutrophilic Stab Cells, %	Segmented Neutrophilic Leukocytes, %	Eosinophils, %	Basophils, %	Lymphocytes, %	Monocytes, %	Termination	Cause of Death	Transfusion Rh+ Cc.	Transfusion Rh— Cc.
3A	3 days	2,800,000	10.4	1.1	7,200	360	..	..	12	59	..	..	17	10	Died 4 days	Br.Pn.	110	...
3B	Birth	1,600,000	7.5	1.4	171,200	376,750	4	4	5	33	3	1	42	8	Survived	.....	135	400
6	5 mo.	1,100,000	4.8	1.3	21,000	3,285	2	..	..	28	4	..	64	2	Survived	.....	225	...
7	3 days	4,100,000	16.0	1.1	31,300	313	..	..	4	72	1	..	15	8	Died 6 mo.	Br.Pn.	...	360
8	4 days	2,700,000	6.6	0.8	17,700	708	8	6	34	40	..	..	2	..	Died 4 days	Purpura	20	...
9	2 days	3,690,000	12.8	1.0	21,400	856	..	..	2	69	1	1	19	8	Died 3 days	Purpura	...	115
10	2 days	4,300,000	15.0	1.0	13,000	2,600	..	..	..	59	..	..	34	7	Died 3 days	Purpura	...	115
11	11 days	1,500,000	6.6	1.3	30,500	5,490	4	3	6	35	2	1	42	7	Survived	.....	350	....
13	5 days	2,800,000	9.0	1.0	22,000	220	..	..	2	78	2	1	10	7	Survived	.....	...	165
14	1 day	4,700,000	18.0	1.1	37,000	1,110	1	..	7	51	2	..	35	4	Died 3 days	Icterus gravis	...	...
15	4 days	1,900,000	9 .0	1.4	15,200	1,368	2	5	6	42	3	1	39	3	Survived	.....	...	275

TABLE 8.—*Summary of Necropsy Findings*

No.	Age	Familial Incidence	Edema	Icterus Gravis	Liver: Hepatomegaly	Liver: Microscopic	Spleen: Splenomegaly	Spleen: Microscopic	Placenta: Enlarged	Placenta: Microscopic
1	Premature stillbirth (970 Gm.)	+	4+ (hydrops)	—	—	+*	— (1.5 Gm.)	+	1:1.3 †	+
4	Stillbirth at term (2,800 Gm.)	+	4+ (hydrops)	—	—	+	+ (20 Gm.)	+	1:1.7	+
3A	4 days	—	+	+	—	+	+ (33 Gm.)	+	..	..
7	6 months	—	—	+	—	—	—	+	..	..
8	4 days	+	—	+	—	+	—	+	..	..
9	3 days	+	+ Local	+	—	+	+ (19 Gm.)	+	1:3.7	—
10	3 days	+	+ Local	+	+	+	+ (15.5 Gm.)	+	1:3.7	—
14	3 days	—	—	+	—	+	+ (22.5 Gm.)	+	..	..

* + indicates findings generally considered as characteristic for fetal erythroblastosis, hemopoiesis, biliary stasis and hemosiderosis.
† Ratio of weight of placenta to body normally about 1:7.

O Rh positive, the mother O Rh negative with anti-Rh agglutinins, baby 1 (a girl) O Rh positive, baby 2 (a boy) O Rh positive. The hematologic data are given in table 6, the necropsy findings in table 8.

An attempt was made to correlate the anemia in the first blood count and the transfusions with the outcome (table 7). The red counts in millions in those that survived were 1.1, 1.5, 1.6, 1.9 and 2.8 and in those that died 2.7, 2.8, 3.6, 4.1, 4.3 and 4.7. The apparent relation between the severity of the anemia and the outcome may be purely accidental in the small series. The effect of transfusions is evident from the following figures: The 5 infants that died received altogether 110 cc. of Rh positive blood, 230 cc. of Rh negative blood and 20 cc. of probably Rh positive blood, together 360 cc. of blood. The 6 children that survived (among them is included child 7, which lived six months) received 1,200 cc. of Rh negative blood and 610 cc. were the second children in the families, the first having been normal. One was the first live born child, preceded by an abortion. In addition to the 2 previously mentioned with severe general hydrops, 3 had moderate local edema and 3 had no edema. Six had severe jaundice of icterus gravis type. Only 1 had an enlarged liver, 150 Gm., with a body weight of 2,640 Gm. The normal weight would be about 106 Gm. In some of the others clinical records referred to palpably enlarged liver. In case 7, necropsy at the age of 6 months showed a liver actually smaller than normal, 136 Gm. as compared with 200 according to body weight of 6,000 Gm. All except case 7 showed microscopic changes (hemopoiesis, hemosiderosis and biliary stasis) in the liver. The child listed as case 7 died at the age of 6 months. That circumstance may be responsible for absence of changes in the liver. Five had splenomegaly, all 8 showed microscopic changes in the spleen

(hematopoiesis and hemosiderosis), 6 showed focal hemopoiesis in other organs, including the kidneys and adrenals. There was nuclear jaundice in the brain in 4. The placentas were examined in only 4, and all were enlarged. Two with considerable enlargement (relation of weights of placenta to body was 1:1.3 and 1:1.7 instead of the normal average of 1:7) showed characteristic microscopic changes (fibrosis, edema, hemopoiesis). The other 2 with moderate enlargement (1:3.7) showed no microscopic abnormalities.

PATHOGENESIS OF FETAL ERYTHROBLASTOSIS

The diversity of findings in fetal erythroblastosis becomes less bewildering when viewed against the background of the genesis of its manifestations. The accompanying diagram attempts to give a genetic concept based on Levine's hypothesis that passage of Rh antibodies from an Rh negative mother to the Rh positive fetus is responsible for the hemolytic anemia in the latter. All the other manifestations are logical sequelae in keeping with our knowledge of similar changes in other conditions. This concept was developed in greater detail in a previous publication.[3] The damage of the liver is placed in the center of the picture, the hemolytic anemia and anoxemia being the fundamental preliminary changes, the other changes resulting from it. The arrows show the course and sequence of events.

There still remains the question why children with various manifestations of the disease are born in the same family. How can it be explained that 1 child has congenital hydrops, another congenital anemia and the third icterus gravis? The order is not necessarily from the least severe form (anemia) to the most severe (hydrops). Four points attempt to answer this question:

CONDITIONS INFLUENCING SEVERITY OF FETAL ERYTHROBLASTOSIS AND ITS MANIFESTATIONS

1. Age of fetus when Rh antibodies begin to act on it.

2. Length of time during which fetus is exposed to such action.

3. Strength of Rh antibodies of which the titer of anti-Rh agglutinins in the blood of the mother may or may not be a measure. There is evidence available suggesting that there is no direct relation between the titer of these antibodies in the mother and the severity of the disease in the baby. However, this needs to be investigated on larger material.

4. Permeability of the placenta. It is possible that there are quantitative differences in different women and at different times even in the same woman.

CONCLUSIONS

Hemolytic anemia due to the action of Rh antibodies is not only the initial cause of fetal erythroblastosis, but it explains the genesis of the complex manifestations of the disease. Damage of hepatic parenchyma is the fundamental change.

The finding of the characteristic distribution of the Rh factor (father and child Rh positive, mother Rh negative) may be used as corroborative evidence favoring the diagnosis of erythroblastosis, but it should not be used as such to the exclusion of other diagnostic criteria. The supportive evidence is greater when anti-Rh agglutinins are found in the Rh negative mother.

ABSTRACT OF DISCUSSION

Dr. A. G. Foord, Pasadena, Calif.: Dr. Fisk in our laboratory demonstrated that the blood of all newborn babes is Rh positive if antiserum produced in guinea pigs by injection of monkey blood is used for the tests. Consequently serums of human origin are essential, and several serums should be used, all of which should be tested against sufficient bloods to determine their subtype. Recently we had the problem of studying a physician's wife who was pregnant. She had had one normal child and then one stillborn with hydrops, at which time she had weak anti-Rh agglutinins in her blood. During this, her third, pregnancy we examined her blood for anti-Rh agglutinins at various intervals, including just before delivery, and were never able to demonstrate any agglutination of Rh positive red cells from several adult persons. She delivered an anemic, full term, living baby with all the findings of erythroblastosis. Multiple transfusions from Rh negative donors saved the child. We had saved the serums from the mother and repeated the agglutination tests with cord bloods obtained from newborn infants. By this method agglutinins were easily demonstrated. I have no explanation for this phenomenon, but as a certain number of women who have delivered babies with erythroblastosis become pregnant subsequently the demonstration of anti-Rh agglutinins in these women's bloods can best be done by using cord bloods.

Dr. Israel Davidsohn, Chicago: Dr. Foord reveals a source of false positive tests if an anti-Rh guinea pig immune serum is used. With such serum the blood of all newborn babies is Rh positive, whereas with human anti-Rh serum the incidence of Rh negative reactions in the blood of newborn babies is similar to that in adults. For the present, human anti-Rh serum is preferable for clinical work. It is advisable to use three immune serums, differing in their specificity. At least one of them should react with about 85 per cent of the population. False results are dangerous. A false positive result may prompt use of an Rh positive donor for an Rh negative recipient and be responsible for a transfusion reaction. False negative results may lead to selection of incompatible donors and also to a wrong conclusion in the interpretation of a so-called bad obstetric history. One may be able to prognosticate to some extent regarding the probable occurrence of erythroblastosis in future pregnancies, by examining all living children. If one of them is Rh negative, the father is heterozygous Rh positive and his children have an even chance to be Rh positive or Rh negative. The Rh negative children will be free of erythroblastosis, at least as far as it is due to the Rh factor. Similar information is sometimes obtainable by examining the husband's parents. If one of them is Rh negative the inference is justified that the husband is heterozygous Rh positive. The relation between the Rh factor in the baby and erythroblastosis has been dramatically illustrated by several reports of erythroblastosis in Rh positive infants, while the Rh negative twins were free of disease. The best time to test for anti-Rh agglutinins in the blood of mothers of babies with erythroblastosis is not immediately after delivery but about ten days later. It is probable that, until birth, there is an interchange of antigenic substances and antibodies between mother and baby. The baby's antigenic substances may neutralize the specific antibodies in the blood of the mother. This explains the higher titer, after an interval of from ten to fourteen days since delivery, when possibility of neutralization has been eliminated.

Earliest Medical Reference Relating to a Miner.—The earliest medical reference which may be interpreted as relating to a miner is to be found in the Corpus Hippocraticum. In the fourth book of Epidemics the following case history is to be found: A man from the mines had the right hypochondrium distended. His spleen was enlarged, and his abdomen was distended and hard. His respiration was labored, and he was both pale and livid. The disease then attacked the left knee. There was a relapse in the entire body and finally a crisis.—Rosen, George: The History of Miners' Diseases, New York, Schuman's, 1943.

ADMINISTRATION OF PENICILLIN BY MOUTH

PRELIMINARY REPORT

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The view is generally held that when given by mouth penicillin is destroyed by stomach acid and in consequence only very small amounts can be detected in the urine.[1] In contrast, when given by intravenous or intramuscular injection, urine recoveries of penicillin were reported to average approximately 60 per cent.[1] Combined administration of penicillin and sodium bicarbonate was followed by the appearance of penicillin in the blood. The detectable levels were, however, found to be very low.[2] In subjects suffering from achlorhydria accompanying pernicious anemia the urinary excretion of penicillin given by mouth reached relatively high figures with appreciable blood levels (up to 40 per cent).[2]

In the light of all these observations, Charney, Alburn and Bernhart[3] studied penicillin excretion through the kidneys after combined administration of penicillin and buffer salts with a buffering range not reaching alkaline p_H values. It is known that penicillin is sensitive not only to acid but also to alkaline reaction. Thus the use of sodium bicarbonate or similar alkaline antacids was considered undesirable and unpractical.

Trisodium citrate was found by Charney, Alburn and Bernhart to be a suitable buffer with the proper buffering range. Administration of 1.0 to 5.0 Gm. of trisodium citrate and 20,000 to 30,000 units of penicillin (both dissolved in 200 to 400 cc. of water) by mouth given two hours after breakfast resulted in appreciable increase of the urinary excretion of penicillin when compared with control experiments in which no buffer was used. The figures for urinary excretion of penicillin given by mouth on a fasting stomach were only slightly increased by the simultaneous administration of buffer and were higher than in the experiments in which penicillin was given after breakfast.

The results of these investigations stimulated the extension of the studies in the clinical field with special reference to the therapeutic possibilities, and the blood levels of penicillin when given by mouth with and without buffer (sodium citrate).

Figures of urinary excretion of penicillin are not an accurate yardstick of the therapeutic effect penicillin might exert while passing through the body. On the other hand, the fact that penicillin given by mouth appears in the urine proves that it is absorbed from the gastrointestinal tract.

Gonorrhea offered the best approach for the therapeutic evaluation of penicillin when given by mouth. The rapid cure of gonorrhea by injected penicillin gave a reliable basis of comparison. If it is effective at all, rapid therapeutic effects would be expected after oral administration of penicillin. Even an unsuccessful attempt would cause no significant delay or harm and could be quickly followed by well established therapeutic procedures.

THE TREATMENT OF GONORRHEA

Table 2 contains the summary of observations on 18 male adults and on 5 children (girls, 3 weeks to 6 years) in whom gonorrhea was treated with penicillin given by mouth. The majority of these cases was resistant to sulfonamides. The doses of penicillin varied from 10,000 units (every three to four hours) in children to 15,000 to 40,000 units (every three hours) in adults for two to three days in combination with trisodium citrate (1 to 5 Gm. per dose). In all these cases cure was achieved in one to three days and with doses which appear to be comparable to, and not out of line with, the customary doses of penicillin when given by injection. It appears, therefore, that penicillin, at least in combination with a buffer such as sodium citrate, is an effective therapeutic agent against gonorrhea, even when given by mouth.

TABLE 1.—*Serum Penicillin Levels*

Units of Penicillin	Vol. of Standard or Serum, Cc.	Broth to 1.0 Cc.	Conversion Factor	Standard 0.05 Unit per Cc. Broth: Read 8 a.m.	Standard 0.05 Unit per Cc. Broth: Read 10 a.m.	Unknown Serum: 8 a.m.	Unknown Serum: 10 a.m.
0.05	1.0	0	1	—	—	—	—
0.04	0.80	0.20	1.25	—	—	—	—
0.03	0.60	0.40	1.66	—	—	—	—
0.02	0.40	0.60	2.5	—	—	—	—
0.01	0.20	0.80	5.0	+	4	—	—
0.0075	0.15	0.85	6.66	+	4	—	—
0.005	0.10	0.90	10	+	4	—	—
0.0025	0.05	0.95	20	+	4	+	4
0.001	0.02	0.98	50	+	4	+	4

Controls: 1. Plain broth + streptococci = growth
2. Serum — no streptococci = no hemolysis
3. Erythrocytes — no streptococci = no hemolysis
4. Erythrocytes + streptococci = 4 hemolysis

— = no hemolysis; 4 = complete hemolysis.

The amounts of penicillin and of sodium citrate used as well as the type of buffer salt may undergo modifications in the future, depending on the outcome of continued and extended investigations. In this connection, observations made on 3 girls (2 to 5 years) not included in table 2 are important. In these 3 patients the administration of 10,000 units of penicillin (every four hours) given with 1 or 2 Gm. of sodium citrate with a total dose of 200,000 to 300,000 units was followed by prompt but only temporary clinical cure of the gonorrhea. The treatment was repeated twice with identical temporary results. The same doses of penicillin given intramuscularly (every three hours) resulted in permanent cure in these 3 children. Thus, either the doses were too low in oral administration or the oral treatment should have been continued over a longer period and with perhaps

This paper was presented, in abbreviated form, by one of us (P. G.) on Dec. 5, 1944 at the postgraduate course in internal medicine (Pediatric Section) of the American College of Physicians, Philadelphia.

The penicillin was provided by the Office of Scientific Research and Development, from supplies assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council.

From the Department of Pediatrics, University of Pennsylvania School of Medicine; Wyeth Institute of Applied Biochemistry, Philadelphia; University Hospitals, Department of Surgery, Western Reserve University School of Medicine and City Hospital, Department of Pediatrics, Cleveland.

1. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Distribution of Penicillin, J. Clin. Investigation **22**: 425-437, 1943.
2. Rammelkamp, C. H., and Helm, J. D., Jr.: Studies on the Adsorption of Penicillin from the Stomach, Proc. Soc. Exper. Biol. & Med. **54**: 324-327, 1943.
3. Charney, J.; Alburn, H. E., and Bernhart, F. W.: Urinary Excretion of Penicillin in Man After Oral Administration with Gastric Antacids, Science, to be published.

administration at shorter intervals. It is of interest to note that these relapses on oral medication occurred in chronic gonorrhea in young girls, whereas gonorrhea in adults seemed in these studies to present less difficulties.

Penicillin, in combination with sodium citrate, given by mouth, caused rapid and permanent cure of gonorrheal conjunctivitis in 3 treated infants (aged 7, 17 and 40 days). The doses used were 10,000 units of penicillin and 1 Gm. of sodium citrate every three to four hours with a total dose of 140,000, 180,000 and 200,000 respectively. The effect was always very prompt and smears became negative after three to four doses.

TREATMENT OF OTHER DISEASES

In a 7 year old girl with nonspecific streptococcic vaginitis penicillin (10,000 units) with 2.0 Gm. of sodium citrate every three hours given by mouth in a total dose of 200,000 units was followed by rapid and permanent cessation of discharge.

In a 3 year old boy suffering from chronic otitis media with perforation and suppuration (hemolytic streptococcus) treatment with sulfathiazole (an initial dose of 2.0 Gm. and then 0.5 Gm. every four hours for twenty-three days) was of no avail. Penicillin combined with 2.0 Gm. of sodium citrate given by mouth 10,000 units every three hours for twenty doses brought about complete cure, as evidenced by complete disappearance of discharge.

In 1 patient with early acquired syphilis and positive dark field examination [4] the combined administration of penicillin (30,000 units every three hours) and sodium citrate (5 Gm. per dose) by mouth did not differ in its result materially from that which ordinarily follows parenteral administration of penicillin. Treponema pallidum decreased in number at eighteen hours. At twenty-four hours only a few distorted organisms were seen and in thirty hours dark field examination was completely negative. At the end of the second day treatment was changed to the standard scheme of intramuscular administration.

All the foregoing preliminary and scattered observations support the conclusions that, even apart from gonorrhea, penicillin given by mouth, in combination with a buffer salt such as sodium citrate, can and does exert a beneficial therapeutic effect comparable in speed to parenteral administration.

In the light of these clinical results the figures for urinary excretion of penicillin gain more practical significance. In this connection it should be noted that, according to a recent publication [5] which appeared after the present clinical and experimental studies were concluded, 8 to 33 per cent of 100,000 units of penicillin given by mouth to normal human subjects, without added buffer, was found to be excreted in the urine. Simultaneous administration of sodium bicarbonate had decreased the figure for urinary excretion, probably because of destruction of penicillin in the alkaline medium of the gastrointestinal tract.

It was expected that valuable information could be gained from following the blood level figures for penicillin after oral administration. Such blood tests taken in hourly intervals after ingestion of penicillin will also illustrate the shape of the blood penicillin curve and its duration.

Among the methods advanced for the assaying of small quantities of penicillin in body fluids are those proposed by Rammelkamp,[6] Wilson [7] and Rake and Jones,[8] which differ somewhat in detail but are all

TABLE 2.—*Patients Treated with the Combination of Penicillin and Sodium Citrate (5 Gm. per Dose) Administered by the Oral Route*

No.	Name	Sex	Diagnosis	Proof by	Dosage, Units	Total Dose Given, Units	Results
1	W. D.	♂	Gonococcic urethritis	Smear	15,000 q 3h × 16	240,000	Clinical cure
2	R. C.	♂	Gonococcic urethritis	Culture	15,000 q 3h × 16	240,000	Clinical cure; cultures negative
3	P. H.	♂	Gonococcic urethritis	Smear	20,000 q 3h × 16	320,000	Clinical cure
4	M. D. H.	♂	Gonococcic urethritis	Smear	15,000 q 3h × 16	240,000	Clinical cure
5	E. V.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 16	320,000	Clinical cure; discharge stopped in about 16 hours; culture negative
6	S. J.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 16	320,000	Clinical cure; culture negative after 24 hours
7	M. C.	♂	Gonococcic urethritis	Smear	20,000 q 3h × 16	320,000	Clinical cure
8	W. R.	♂	Gonococcic urethritis	Smear	20,000 q 3h × 24	480,000	Clinical cure
9	R. P.	♂	Gonococcic urethritis with periurethral abscess plus perineal urethral fistula	Culture	15,000 q 3h × 16	240,000	Clinical cure; culture became negative
	Readmitted 2 weeks later			Culture	20,000 q 3h × 24	480,000	Clinical cure; culture became negative
	Checked 3 weeks later			Cultures and smears at repeated examination (5 ×) found negative; the persisting slight (gonococcic negative) discharge was considered to be due to his abnormal urinary tract			
10	M. H.	♂	Gonococcic urethritis and epididymitis	Culture	20,000 q 3h × 16	320,000	Clinical cure within 24 hours
11	K. T.	♂	Gonococcic urethritis	Smear	40,000 q 3h × 12	480,000	Clinical cure
12	A. B.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 16	320,000	Clinical and bacteriologic cure
13	O. M.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 24	480,000	Clinical cure; culture became negative on the third day of treatment
14	C. B.	♂	Gonococcic urethritis	Smear	40,000 q 3h × 12	480,000	Clinical cure
15	J. G.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 16	320,000	Clinical and bacteriologic cure
16	E. P.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 16	320,000	Clinical and bacteriologic cure
17	T. B.	♂	Gonococcic urethritis	Smear	20,000 q 3h × 16	320,000	Clinical cure
18	C. T.	♂	Gonococcic urethritis	Culture	20,000 q 3h × 16	320,000	Clinical and bacteriologic cure
19	D. L.	♀, 4½ yr.	Gonococcic vaginitis	Smear	10,000 q 3h × 30*	300,000	Clinical cure in 24 hours
20	V. A.	♀, 4¾ yr.	Gonococcic vaginitis	Smear	10,000 q 3h × 20*	200,000	Clinical cure in 24 hours
21	D. H.	♀, 3 yr.	Gonococcic vaginitis	Smear	10,000 q 3h × 20†	200,000	Clinical cure
22	D. L. B.	♀, 6 yr.	Gonococcic vaginitis	Smear	10,000 q 4h × 20*	200,000	Clinical cure
23	J. G.	♀, 3 wks.	Gonococcic vaginitis	Smear	20,000 q 4h × 12*	240,000	Clinical cure

* Received only 2 Gm. of sodium citrate with each dose of penicillin.

† Received only 1 Gm. of sodium citrate with each dose of penicillin.

4. This observation was kindly put at our disposal by Dr. H. N. Cole and Dr. G. W. Binkley, University Hospitals, Cleveland.

5. Free, A. H.; Leonards, J. R.; McCullough, D. R., and Biro, B. E.: The Urinary Excretion of Penicillin After Oral Administration to Normal Human Subjects, Science **100**: 431-432, 1944.

6. Rammelkamp, C. H.: A Method for Determining the Concentration of Penicillin in Body Fluids and Exudates, Proc. Soc. Exper. Biol. & Med. **51**: 95-97, 1942.

7. Wilson, C.: A New Rapid Method for Penicillin Assay, Nature, London **152**: 475, 1943.

8. Rake, G., and Jones, H.: A Rapid Method for Estimation of Penicillin, Proc. Soc. Exper. Biol. & Med. **54**: 189-190, 1943.

based on the inhibition of hemolysin production by a selected strain of streptococcus.

The sample protocol (table 1) illustrates the procedures used in these investigations.

The following modifications were incorporated in our procedures:

1. The total volume of serum required was more than in other methods, but a greater accuracy was obtained.

2. The broth used consisted of 2 per cent Difco Tryptose, 1 per cent neopeptone, 0.85 per cent sodium chloride, p_H 7.2.

3. The test organism was a group A hemolytic streptococcus, number C203, grown for eighteen to twenty hours on 1.0 per cent horse serum agar of the foregoing medium. The organisms were washed twice with 0.85 per cent saline solution to remove all traces of hemolysin. A final inoculum of from 5,000 to 10,000 organisms per tube was sufficient.

4. Initial tests indicated a lysis of both rabbit and sheep erythrocytes by complement in the serum samples. Substitution of human type O erythrocytes worked very satisfactorily.

5. The inoculum consisted of 1 cc. of 4 per cent erythrocytes, washed twice with isotonic solution of sodium chloride and 5,000 to 10,000 streptococci, giving a final volume, with the 1.0 cc. serum dilution, of 2 cc. per tube.

6. Incubation at 37 C. proceeded for sixteen to eighteen hours.

7. Initial readings were made without shaking the tubes. After thorough resuspension of the erythrocytes and two additional hours of incubation, final readings were made. Complete hemolysis in tubes containing insufficient penicillin was the usual rule. Incomplete hemolysis at the second reading in 1.0 cc. serum tubes, in comparison to complete hemolysis in the standard series, was considered as indicative of a trace of penicillin, although, if allowed to incubate longer, such tubes eventually showed complete hemolysis. In agreement with Rammelkamp, the tubes showing no hemolysis were sterile.

8. Potencies were obtained by multiplication of the lowest unitage of standard penicillin showing a negative tube times the conversion factor of the smallest volume of active sample as in the protocol; i. e., $0.02 \times 10 = 0.20$ unit of penicillin per cubic centimeter of serum.

TABLE 3.—*Patients After Overnight Fasting*

Penicillin Given by Mouth Thirty Minutes before Breakfast (Cereal, Cream, Sugar, Toast, Butter, Egg, Milk)

No.	Name	Age	Diagnosis	Calcium Penicillin, Units: With Buffer	Calcium Penicillin, Units: Without Buffer	Blood Levels—Units per 100 Cc. Serum Hours after Ingestion of Penicillin: 1	2	3	4
1	J. G.	8 yrs.	Postoperative appendectomy	40,000	.....	15	7.5	3.75	None
2	D. D.	9 yrs.	Concussion	.....	40,000	3.75	None	None	None
3	M. L.	9 yrs.	For study	40,000	.....	7.5	3.0	Trace	Trace
4	L. M.	9 yrs.	Rheumatic heart	.....	40,000	7.5	None	None	None
5	L. S.	11 yrs.	Postpoliomyelitis	40,000	.....	5.0	2.5	Trace	Trace
6	R. G.	12 yrs.	Postpoliomyelitis	.....	40,000	2.5	Trace	Trace	None
7	E. O.	6 yrs.	Tracheotomy	40,000	.....	20	10	5	Trace
8	D. W.	6 yrs.	Postoperative tonsillectomy and adenoidectomy	.....	40,000	5	2.5	Trace	None
9	L. G.	12 yrs.	Rheumatic heart	40,000	.....	10	3.3	2.5	2.5
10	J. D.	2 yrs.	Diabetes mellitus	.....	40,000	Trace	Trace	None	None
11	J. G.	3 wks.	Gonococcic vaginitis	20,000	.....	100	40	20	20
12	M. B.	4 wks.	Rickets	.....	20,000	20	3.3	None	None

TABLE 4.—*Patients After Overnight Fasting*

First Meal Given Four Hours after Penicillin (by Mouth)

No.	Name	Age	Diagnosis	Calcium Penicillin, Units: With Buffer	Calcium Penicillin, Units: Without Buffer	Blood Levels—Units per 100 Cc. Serum Hours after Ingestion of Penicillin: 1	2	3	4
1	T. M.	9 yrs.	Chronic nephritis	40,000	.....	2.5	None	None	None
2	G. S.	7 yrs.	Chronic nephritis	.....	40,000	10	2.0	None	None
3	J. G.	7 yrs.	Fractured femur	40,000	.....	10	3.3	2.0	None
4	H. O.	10 yrs.	Chronic osteomyelitis	.....	40,000	2.0	None	None	None
5	L. M.	9 yrs.	For study	40,000	.....	5.0	5.0	3.75	None
6	A. W.	8 yrs.	For study	.....	40,000	7.5	5.0	Trace	None
7	J. C.	8 yrs.	Tuberculosis ?	40,000	.....	10	5.0	2.5	Trace
8	M. F.	7 yrs.	Pneumonia	.....	40,000	7.5	5.0	3.75	3.75
9	A. R.	7 yrs.	Chronic nephritis	40,000	.....	20	2.5	2.0	2.5
10	S. C.	6 yrs.	Postpoliomyelitis	.....	40,000	5.0	Trace	None	None
11	J. B.	7 yrs.	Postappendectomy	40,000	.....	20	7.5	7.5	7.5
12	K. H.	7 yrs.	Postappendectomy	.....	40,000	5.0	None	None	None

The possibility of Rh interference exists but is remote. An alternative method, using sheep erythrocytes, which may be used if human cells are not available, is to heat serum samples in a water bath at 56 C. for five minutes. Control series of standard penicillin in human serum, with or without complement, and in plain broth, demonstrated no destruction of penicillin by this treatment.

No evidence was found in any series of heated or unheated serums against human or sheep erythrocytes, controlled by broth dilutions of standard penicillin, to support the contention of Holmes and Lockwood[9] that human serum contained an antipenicillin factor.

With respect to the high incidence of complement interference in these assays it must be borne in mind that the tests were made on children, in whom the incidence of occurrence of high titer complement may possibly be greater than in adults.

The sample protocol may be extended to include more than 1 unit by diluting serum 1:50 and using volumes decreasing by 0.1 cc. quantities.

With the method used 0.02 unit per cubic centimeter was accurately determined. "Trace" signifies levels between 0.01 and 0.02 unit per cubic centimeter.

In this group of experiments, penicillin calcium was used either in the form of the usual dry preparation in bottle or in the form of tablets especially made up with trisodium citrate (1 Gm. of sodium citrate with 10,000 units of penicillin calcium in one tablet[10]). Each day 2 children of closely similar age and weight received 40,000 units of penicillin, one in the form of a tablet with buffer dissolved in water and the control without buffer in freshly prepared aqueous solution. The results are summarized in tables 3 and 4. When penicillin was given by mouth thirty minutes before breakfast, sodium citrate administered simultaneously increased the abso-

9. Holmes, L. F., and Lockwood, J. S.: Studies on Bioassay of Penicillin, Am. J. M. Sc. **207**: 267-268, 1944.

10. Furnished by Wyeth Incorporated.

lute blood levels and also prolonged the presence of penicillin in the blood. Penicillin could be detected in the blood (with one exception) four hours after ingestion, whereas it is a rarity to find penicillin in the blood even three hours after intramuscular injection of aqueous penicillin solution.[11] When penicillin was ingested after overnight fasting and four hours before the first meal, the effect of the buffer salt was less pronounced but still significant.

The investigations on blood levels of penicillin following its oral administration are being continued under varied experimental conditions. However, the results so far obtained allow a generalization, i. e. ingested penicillin reaches the circulation in therapeutic concentration and in prolonged flow from the intestine.

CONCLUSIONS

1. Penicillin given by mouth in combination with a suitable buffer salt, such as trisodium citrate, was found to be therapeutically effective in a number of cases of gonorrhea and other diseases.

2. The effective doses were comparable to the doses routinely used in parenteral administration.

3. Combination of penicillin and sodium citrate given by mouth produces greater and more prolonged increase of penicillin blood levels than penicillin ingested without a buffer salt.

CURARE IN ANESTHESIA

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Good muscular relaxation is one of the requirements for efficient abdominal surgery, and in order to obtain this relaxation surgeons and anesthetists have sometimes used anesthetic drugs and methods which are toxic or hazardous. The introduction of curare into clinical medicine has made it possible for us to obtain complete muscular relaxation at any time during anesthesia with nontoxic controllable anesthetic agents. After more than two years of careful clinical observation I have come to the conclusion that curare is a safe drug to use in combination with certain anesthetic agents, provided it is administered under properly controlled conditions.

The story of the transformation of this South American Indian arrow poison into an anesthetist's tool may be told briefly as follows: Curare has been known to science since 1595, when Hakluyt referred to it in his description of Sir Walter Raleigh's voyage up the Orinoco. In 1840 Claude Bernard,[1] in a series of famous physiologic experiments, confirmed the observations which Watterton and Brodie had made in 1814, that curare action was paralysis due to interruption of the neuromuscular mechanism. The drug therefore became of value in the physiologic laboratory for the study of muscle activity without interference from nervous impulses. Clinicians had more than once cast hopeful eyes toward the possible use of curare in the treatment of spastic disease of the muscles, but always its poisonous reputation and the presence of cardiac depressants and other adulterants in the available supplies made a clinical trial seem too dangerous. No one knew the exact botanic sources of curare or the chemical composition of its active principle. In 1938 Richard C. Gill,[2] an American who had lived for years in the upper Amazonian jungles of Ecuador and who was familiar with the Indian folklore and mysticism which has surrounded the "flying death," as curare is called in the jungle, brought back to the United States the first adequate supply of the drug with properly labeled specimens of the various plants which are used by the Indians in the manufacture of crude curare. Professor A. R. McIntyre [3] of the University of Nebraska then subjected this supply of curare to the first pharmacologic study by modern methods. Through cooperation with the Research Laboratories of E. R. Squibb and Sons a purified product was produced which exhibited the true curare action without toxic side effects and which seemed safe for human experimentation. The present commercial product, which is known as "Intocostrin" (Extract of Purified Curare, Squibb), is marketed in 5 cc. vials of a pale amber liquid which contains 20 mg. of active curare substance to each cubic centimeter. It is obtained from the single plant Chondrodendron tomentosum and has a selective action affecting first the muscles of the throat and neck, then the skeletal muscles of the extremities, chest and abdomen, and the diaphragm last or not at all. It has no effect on involuntary or cardiac muscle in therapeutic doses.

The first large scale test of the new curare on human subjects was made by Professor A. E. Bennett [4] of the University of Nebraska, who used it to soften the traumatic effects of convulsive shock therapy in psychiatric patients. This use for curare in conjunction with both metrazol and electric shock therapy has become widespread in mental hospitals, and now many thousand injections have been given without harmful effect. With this pharmacologic and clinical evidence of the safety of "Intocostrin" we felt that it might be tried on patients under general anesthesia, and so at the suggestion of Dr. L. H. Wright of New York we began using it in patients under cyclopropane anesthesia at the Homeopathic Hospital of Montreal in January 1942. The results obtained were dramatically successful, but we proceeded cautiously until we became fairly sure that there were no postoperative effects to worry about, and it seemed advisable to publish a preliminary report [5] and to seek confirmation of our results by other workers. The reports which have been published and which have been communicated to me personally by many anesthetists are unanimous that curare has a useful place in anesthesia, and that its use appears to be safe. The most convincing and valuable work which has been done is that of Dr. S. C. Cullen [6] of the State University of Iowa, who has been using curare routinely in abdominal surgery since 1942 and who has now reported over 1,000 successful administrations. I myself have administered curare only 300 times, because I have preferred to give it only to those patients who need extra relaxation and,

11. Romansky, M. J., and Rittman, G. E.: Method of Prolonging Action of Penicillin, Science **100**: 196-198, 1944; Penicillin: Prolonged Action in Beeswax-Peanut Oil Mixture; Single Injection Treatment of Gonorrhea, Bull. U. S. Army M. Dept., 1944, no. 81, pp. 43-49. Rammelkamp and Keefer.[2]

From the Department of Anesthesia, Homoeopathic Hospital of Montreal.

Read before the Section on Anesthesiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

1. Bernard, C.: Note sur la curarive et ses effets physiologiques, Bull. gen. de therap. **69**: 23, 1865.

2. Gill, R. C.: White Water and Black Magic, New York, Henry Holt & Co., Inc., 1940.

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as I will show in my statistics, that is in a comparatively small proportion of our total cases.

I do not propose in this clinical report to discuss the physiologic and pharmacologic action of curare. It is sufficient to state that it acts on the neuromuscular synapse probably by neutralization of the acetylcholine reaction. It effectively blocks synaptic transmission between preganglionic and postganglionic fibers of the sympathetic division of the autonomic nervous system. Curare is eliminated very rapidly, partly by destruction in the liver and partly by excretion unchanged by the kidneys. No evidence of any visceral damage has been produced and no direct effect on the heart reported. It may apparently be given to patients with damaged liver or kidney without any prolongation or intensification of the effect. We have used it on some very poor risk patients quite harmlessly, although the patients for whom it is most needed for relaxation are healthy muscular individuals. Respiratory depression may occur following curare injection and has been noted in about 10 per cent of our cases. However, this is always transitory and may easily be controlled by the same methods which we employ to control respiratory depression occurring from other causes during anesthesia. An overdose causing complete respiratory paralysis can be overcome by artificial ventilation of the lungs with oxygen during the ten or fifteen minutes of paresis. Neostigmine bears a close resemblance to a true physiologic antidote to curare, since it acts to inhibit cholinesterase and restore the acetylcholine preponderance at the myoneural junction. For this reason an ampule of neostigmine should always be available when curare is used, although in our experience it has never been necessary to use it.

Most of the patients to whom I have administered curare have been undergoing abdominal operations under cyclopropane anesthesia. For years I have found cyclopropane unmixed with ether to be generally satisfactory for abdominal surgery, and I have used it in a much larger proportion of cases than do many other anesthetists. I myself have administered cyclopropane over 10,000 times and have been lucky enough to have all these patients leave the operating room alive, but I must admit that there are times when it is difficult to secure complete muscular relaxation with cyclopropane alone. Since we have had curare we do not try to push a resistant patient into deep anesthesia with cyclopropane, but at the first evidence of inadequate relaxation we make an intravenous injection of curare. This takes effect within a few seconds and is usually sufficient when combined with cyclopropane to maintain relaxation as long as it is required during the operation. The duration of the effect of a single dose of curare when not combined with cyclopropane or other anesthetic agent is not more than fifteen or twenty minutes. The accompanying table shows the incidence of our use of curare in 1,000 consecutive operations. It is noted that curare is, as might be expected, more often needed for upper abdominal and for pelvic surgery than for ordinary appendectomies, and in the extra-abdominal cases it has been employed usually to facilitate endotracheal intubation.

There have been some differences of opinion between various workers as to the proper dose of curare to be used for patients under anesthesia. All are agreed that it is best given intravenously, although intramuscular injections are used for the treatment of patients with spastic disease and "Intocostrin" is not irritating to the subcutaneous tissues. The intravenous route secures the most rapid and controllable effect for our purpose. Cullen, and more recently Baird and Adams [7] of the Mayo Clinic, recommend an injection of 2 to 3 cc. of "Intocostrin" after the skin incision is made, to be repeated if muscular relaxation is not satisfactory. My routine has been somewhat different. To the average adult patient I usually give a dose of 5 cc. of "Intocostrin" (100 mg. of curare) in one intravenous injection. This has proved to be adequate in almost every case and has had no harmful effect in any case except occasional respiratory depression, which, as I have said, is easily controlled. It is a simpler method than to give fractional doses according to the patient's requirement, as recommended by Cullen. Too small a dose will lead to disappointing results, as was the case with some of the earlier investigators—it is the old story of sending a boy on a man's errand. The doses being used in psychiatry for the minimizing of convulsion trauma are smaller than we recommend in anesthesia, but I believe that in the operating room with facilities always at hand for the control of respiration the conditions are safer for large dosage than in most mental hospitals. Our patients have varied in age from 12 to 75 years, and the dose should be reduced in proportion to the weight of a child or to factors of frailness and asthenia in the aged. Whether curare can safely be used with babies and quite small children remains to be determined by those who work in that field. I have not used it in any case of cesarean section or obstetric delivery.

One Thousand Consecutive Operations with Curare

Total operations	1,000	Curare used, 86 or 8.6%
Abdominal operations	478	Curare used, 79 or 16.5%
Appendectomies	228	Curare used, 23 or 10.1%
Hysterectomies	67	Curare used, 22 or 32.8%
Gallbladder and stomach	42	Curare used, 19 or 45.2%
Other abdominal	141	Curare used, 15 or 10.6%
Bowel resection	4	
Exploratory laparotomy	2	
Colostomy	2	
Herniotomy	3	
Salpingectomy and the like	4	
Extra-abdominal operations	522	Curare used, 7 or 1.3%
Hemorrhoidectomy	1	
Tonsillectomy	1	
Thyroidectomy	1	
Bronchoscopy	2	
Esophagoscopy	1	
Manipulation of foot	1	

As I have said, almost all our patients have been under cyclopropane anesthesia with no added ether or other anesthetic agent. There is no doubt that curare works ideally in combination with cyclopropane. I think, however, that it may be used safely with other agents, particularly with nitrous oxide and ethylene. Cullen has shown that with ether the dose of curare should be reduced to one third of that usually used during cyclopropane anesthesia. Experimental studies have shown that this is because ether itself has a pronounced curariform action and that the myoneural junction is already partially paralyzed. If this factor is kept in mind curare may be used satisfactorily during ether anesthesia, and relaxation and a quiet abdomen obtained without deep anesthesia.

I have used curare in conjunction with sodium pentothal in only 1 case, but Dr. Fernando Hudon of Quebec, who uses pentothal for much abdominal surgery, has obtained excellent results with the combination of "Intocostrin" and pentothal in a fairly large series of cases.[8] There seems to be no significant change in respiration and pulmonary ventilation with this combination.

7. Baird, J. W., and Adams, R. C.: Curare in General Surgery, Proc. Staff Meet., Mayo Clin. **19**: 193, 1944.
8. Hudon, F.: L'emploi du curare comme adjuvant de l'anesthésie générale, Laval méd. **9**: 242, 1944.

Preoperative medication does not seem to have any effect on curare action. Cullen has stated that atropine or scopolamine is apparently essential in the premedication. Our experience has not borne out this theory, as at least half of our patients have received neither of these drugs, and I can see no difference in the curare action. Nor have we had any special difficulty with hypersecretion of mucus which might be attributed to curare. About 10 per cent of our curare patients received a moderate dose of solution of tribromoethanol previous to cyclopropane, and here again there has been no significant change in the curare effect. The complete absence of all postoperative effects from curare has been one of the most striking and encouraging features of this whole investigation.

Much more clinical and laboratory experience will be needed before we can come to any conclusion as to the permanent place of curare in anesthesiology. However, in view of our experience so far I venture to predict that it will have some effect in reducing the incidence of spinal anesthesia, since the indication for many spinal anesthetics is in order to obtain abdominal muscular relaxation; and also that curare will increase the use of pure cyclopropane or pentothal anesthesia for abdominal surgery without the addition of ether and thus reduce postoperative complications. May I close with an urgent word of caution—curare is still a poison and, like every other poison, it should be handled intelligently and only by experienced physicians.

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ABSTRACT OF DISCUSSION

Dr. Stuart C. Cullen, Iowa City: Although the first enthusiasm for the use of curare as a means of improving muscular relaxation has not yet reached its zenith, it appears likely that this drug, in the purified and standard form known as "Intocostrin," will weather the discredit it will most assuredly receive from indiscriminate users and become a beneficial adjunct to the anesthetist's catalogue of drugs. It seems untenable that a drug with such a lurid history and with so potent an effect should be so incapable of producing acute or chronic damage. Extensive and painstaking investigation of this drug in the past has failed to disclose any injury to tissue except that resulting from asphyxia associated with unrelieved respiratory paralysis. Current clinical and laboratory research with the more purified form of curare has not altered the conception of any of the significant features of the action of the drug. These later inquiries have corroborated the innocuousness of the drug in its action on the heart, the peripheral circulation, the liver, the kidney and the striated muscle. This lack of positive findings does not, however, belittle the necessity for continued close scrutiny of the action of curare in the clinic and in the laboratory. It is still necessary to know its effect on the smooth muscle, its placental permeability, its effect on the constituents of the blood, its effect on cortical and medullary cells and its ultimate effectiveness in improving the anesthetic technic so that more patients will return home sooner and in better shape. With the exception of Dr. Griffith's technic of administration, I am thoroughly in accord with all that he has said. On principle, I object to the injection of the same dose to all persons of the same age or physical state without regard to the particular demands of the situation. There cannot help but be overdosage in some instances and underdosage in others. Fortunately, overdosage produces minimal hazard if one is prepared to combat the momentary respiratory paralysis, and no one should employ curare without being so prepared. The chief advantage of curare lies in the fact that its use permits the employment of relatively nontoxic and readily controlled anesthetic agents and technics. Any reduction in morbidity or mortality that may attend the use of curare during anesthesia will be only a reflection of the anesthesiologist's ability to adapt less toxic and more facile agents and technic to the more difficult anesthetic problems.

Dr. J. W. Baird, Minneapolis: Although curare is a potent poison in large doses, it is proving to be a safe drug when used intelligently. Apparently there is but one absolute contraindication to its use: the inability of the anesthetist to perform artificial respiration adequately and thus successfully combat the respiratory failure which we at times encounter. This point cannot be too strongly stressed. If the drug is to fall into disrepute, I feel that it will be because the anesthetist has not availed himself of the proper apparatus and knowledge to treat the respiratory failures. Profound anesthesia is not used from choice, but rather from necessity, if we are to produce adequate muscular relaxation for abdominal surgery. The profound anesthesia is frequently as shock producing as the surgery itself; however, curare has to a large extent eliminated the necessity of the deeper stages of anesthesia and its accompanying dangers. If there is an advantage in the lighter planes of anesthesia—and I definitely feel that there is—I believe it is advisable to use the drug more or less routinely rather than to rely on it only for the occasional case in which difficulty is encountered in producing relaxation by the usual methods. Consequently we are seeing a better convalescence in the patient who has received curare and has been spared a long profound general anesthesia. Cyclopropane is perhaps the anesthetic agent of choice; although we have used the other anesthetic agents with no untoward results. My associates and I give curare in smaller, divided doses. By adhering to this technic we are avoiding the severe respiratory depressions we see when a large dose of the drug is administered. Granted that this depression is easily controlled by compressing the breathing bag on the gas machine, we feel that it is advisable to avoid this depression if possible and still successfully produce the muscular relaxation needed. Usually the greatest muscular relaxation is needed for opening and closing the abdomen and at the time of exploration. After the exploration is completed and the packs and retractors are in place, a high degree of muscular relaxation is usually unnecessary for good operating conditions. Frequently the initial dose of curare is adequate until the abdomen is to be closed. At this point a supplementary injection is made. However, a smaller dose of the drug is usually adequate for the closure. This dose is frequently 15 to 20 mg. smaller than the initial dose. In a survey recently made at the University of Minnesota Hospitals it was found that the average period of time between the first and second dose of the drug was seventy-five minutes. Another use we have found for the product is for the patient who is resistant to the anesthetic agents. This type of patient is usually heavy and muscular and frequently is a heavy drinker and smoker.

Dr. H. R. Griffith, Montreal: I gave the impression, perhaps, that I always use 5 cc. of "Intocostrin." That is the usual dose for an average person. If a patient is small or frail, I sometimes go down to 2 or 3 cc. It is a somewhat easier technic to give 5 cc. (100 mg. of drug) in one dose than waiting to see if 2 or 3 cc. is effective and then giving another injection after one sees that the first is not sufficient. There is a question as to whether curare has any anesthetic action. Theoretically I would say no, and I would not recommend it to be used as an anesthetic in any way. There is some evidence, however, that curare in large doses may have an anesthetic action; at least it will produce unconsciousness. Dr. Rolland Whitacre of Cleveland tells me that he has some experience which shows that a patient can be put to sleep with curare alone if he is given enough, without any other anesthetic agent. But that isn't a technic of anesthesia that any of us recommend, and I know he doesn't. Curare is useful in difficult cases for bronchoscopy. A dose of curare for a perfectly conscious patient is a rather terrifying procedure, that is, an ordinary dose of 3, 4 or 5 cc. of "Intocostrin," because he is not asleep and he gets a relaxation of his throat and neck, and he thinks he is going to die. But if you are going to do a bronchoscopy on a patient who is well sedated and who has also had curare he will have the bronchoscope in his throat anyway, and he won't have time to think about how unpleasant it is to have relaxation of the throat and neck. In the use of this agent, as well as any other agents or methods, the anesthetist is more important than the agent that is being used, and curare may be very dangerous in the hands of untrained personnel.

Clinical Notes, Suggestions and New Instruments

FULMINATING MENINGOCOCCEMIA (WATERHOUSE-FRIDERICHSEN SYNDROME)

AN UNUSUAL CASE WITH RECOVERY FOLLOWING TREATMENT WITH PENICILLIN

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The Waterhouse-Friderichsen syndrome is designated as a symptom complex characterized by purpura and shock associated with the postmortem findings of bilateral adrenal hemorrhage. Karsner [1] states that this syndrome may be caused by the streptococcus, pneumococcus or influenza bacillus. Boger [2] cites a case in which meningococci were demonstrated by direct examination of the peripheral blood smear. He states that this finding has been recorded as occurring only in fatal cases.

In this case the pathologist demonstrated meningococci in the smear after repeated examinations. Boger's report would indicate that this is the first surviving patient in whom the meningococcus was demonstrated in the peripheral blood smear.

Cosgriff [3] states that with the increasing prevalence of meningococcic meningitis there was an associated rise in the number of cases of the so-called Waterhouse-Friderichsen syndrome. He cited 4 adult cases seen in the New York Presbyterian Hospital in the course of eight months. Up until 1942 only 103 cases had been reported, with apparently three recoveries. Ninety per cent of these were in infants or children under the age of 9 years. Cosgriff describes the postmortem findings as characterized by invariable hemorrhage into the adrenals, frequent hemorrhage into the skin, muscles, brain and other organs, focal necrosis of the liver, myocarditis and acute splenic tumor. He states that the infection causing this syndrome is often so overwhelming in nature that early recognition is important so that treatment may be prompt. In the majority of reported cases death has occurred within twenty-four hours after the onset.

Herrick [4] says that most of the meningococcic infections are bacteremic before they attack the leptomeninges. In speaking of this syndrome associated with meningococcic infection he says "No other infection so quickly slays."

Martland,[5] in reviewing 19 autopsy cases, states that the medical history and clinical data obtained were not sufficiently comprehensive because death occurred so soon after the onset of the illness.

The most common symptoms they record are headache, vomiting, gastrointestinal symptoms, fever, chills, abdominal pain, general pain over the entire body, cyanosis and ecchymotic and purpuric spots varying in size from small petechiae to large areas, often confluent and forming a maculopurpuric rash over the body. The skin lesions may develop over the body even while the patient is being examined. The patient becomes rapidly worse in a few hours and soon becomes mentally confused, delirious and moribund. Frequently the pulse is imperceptible but may reach 200. The blood pressure may drop to 60 or 50 in a short time. The leukocyte count recorded in 5 cases ranged from 20,200 to 99,500. Positive blood culture was present in only a few cases. In these 19 cases of Martland's, meningococci were obtained from the petechiae in 2 cases. In 5 of these 19 cases intravenous injections of sodium sulfadiazine and dextrose were given with no apparent change in the course of the disease. Intravenous saline solution and adrenal cortex extract were tried in 5 cases with no apparent result. There was massive hemorrhage of the adrenals in all the typical cases. They stated that bullous lesions with necrosis of the skin were reported and gangrene of the toes or the whole extremity may occur rarely. Bernstein [6] cited only 1 case in the literature in which gangrene of the toe or causalgia accompanied meningococcic meningitis.

In the report made by Martland in February 1944 he states that the Waterhouse-Friderichsen syndrome is apparently that of a fatal infection with a duration of from eight to forty-eight hours from the time of onset, that it is doubtful whether any patient recovers and that death is due to an overwhelming meningococcic infection rather than to insufficiency of the adrenal cortex.

Herrick believes that the meningococcic infection has a selective affinity for the delicate capillary endothelium of the adrenal. Cosgriff as late as August 1944 suggested that penicillin might prove valuable for the treatment of this condition.

REPORT OF CASE

A white woman aged 27, a schoolteacher, awakened on Aug. 22, 1944 with a slight sore throat. At dinnertime she had a slight headache and went to bed early. At midnight she began to vomit and complained of pain over the body, especially in the abdomen. When I saw her, about 4 a. m., the patient was still vomiting a little; she had pain in the abdomen but there was no definite localization of pain or rigidity. The tenderness was about the same over the left kidney area as over any other part of the abdomen. There were no marks on the body anywhere at this time, which was about 4:30 in the morning, or about four and one-half hours after the onset of the illness. She complained of pain on motion or pressure over the extremities and abdomen. She appeared dazed or mentally confused, answering questions slowly and hesitatingly, and no definite source of the manifest toxicity could be determined.

The possibility of a ruptured appendix was considered, although the period of time from onset of the illness seemed too short for this condition. That she might be taken into a hospital quickly, a ruptured appendix was given as a provisional diagnosis. At about 4:30 a. m. arrangements were made for her to go to the hospital as soon as possible. She arrived in the hospital at 7:30 a. m. The sister in charge telephoned when the patient reached the hospital to say that there was an extensive eruption over the body. Later the sister said that, from the time she went to make the call until she returned to the patient, the purpuric spots had increased noticeably. The patient's mother then volunteered the information that these purpuric spots began to appear about 5 a. m., starting on the right thigh and extending distally with great rapidity. She stated that these spots "popped out just like corn popping." At 9 a. m. the purpuric blemishes of varying size were very extensive over the body; only a few small petechiae appeared on the face. On the upper areas of the body and the upper extremities, the eruptions were larger than those on the face. On the knees, legs and feet there were many large areas with what appeared to be thrombotic centers. Both the great toes and several of the small toes seemed almost gangrenous at this time. At the dorsal area of each foot a purplish discoloration extended proximally from the base of the toes.

The patient had a slightly loose stool. This indicated the possibility of an intestinal infection. Sulfaguanidine was started at once. Because of the rapid progress of the disease, penicillin was administered, 20,000 units of the substance injected intramuscularly at about 9 a. m. and ordered to be given every four hours, although no laboratory report had yet been received. The pulse and temperature were about normal when the patient was seen at her home. Soon after arriving in the hospital the temperature rose to 102 F. and the pulse rate to 136. Approximately three hours after the second dose of penicillin had been administered the temperature dropped to 99 F., the pulse rate

Read at a staff meeting of St. Luke's Hospital, Pasadena, Calif., during October 1944.

1. Karsner, H. T.: Human Pathology, ed. 6, Philadelphia, J. B. Lippincott Company, 1942, p. 704.
2. Boger, W. P.: Fulminating Meningococcemia, New England J. Med. **23**: 385-387 (Sept. 14) 1944.
3. Cosgriff, S. W.: The Waterhouse-Friderichsen Syndrome: Observations on Associated Adrenal Insufficiency and Report of Four Cases, Ann. Int. Med. **21**: 187-193 (Aug.) 1944.
4. Herrick, W. W., cited by Boyd, W.: Textbook of Pathology, ed. 4, Philadelphia, Lea & Febiger, 1943, p. 857.
5. Martland, H. S.: Fulminating Meningococcic Infection, Arch. Path. **37**: 147-158 (Feb.) 1944.
6. Bernstein, P.: Causalgia and Gangrene: Rare Complications in Meningococcal Meningitis, New England J. Med. **230**: 482-483 (April 20) 1944.

anesthetic problems.

may be very dangerous in the hands of untrained personnel.

to 80. In the meantime the laboratory report arrived and showed a leukocyte count of 9,600; the urine and blood were within the limits of normal.

About midnight the nurse reported that the pulse was weak and irregular and that the patient was restless, was confused and complained of pain in the extremities. Her feet and legs were cold and clammy.

The following day an attempt was made to administer intravenous glucose. The vein was easy to enter, but no solution would flow in, although the blood came out quite readily. The blood pressure had now dropped to 60 and at times was almost unobtainable. After several attempts were made to give intravenous glucose without satisfactory results, an ampule of ephedrine was given. About fifteen minutes later the fluid flowed in freely. From this time on not much difficulty was encountered in giving intravenous solutions. At this time adrenal cortex extract was given. Another report from the laboratory showed that the leukocyte count had risen to 47,000 (this was on the second day).

On the third day the patient began to bleed from the nose and the vagina. This was about two weeks from her normal menstrual period. The bleeding was not excessive, but 3 cc. of a hemostatic was given in the hope that it might serve to check hemorrhage from the adrenals. The external bleeding stopped promptly. The patient showed some improvement from the third day on, and on the fifth day there was a decided improvement in her general condition. Several toes were now definitely gangrenous, and many large ulcerated areas were present on the knees, legs and feet. In the centers of these large, ulcerated areas were gangrenous regions, some of them 2 or 3 cm. in diameter. The only one located above the knees was on the right buttock. The temperature rose to 103 F. at this time. This was probably due to the infection in these gangrenous areas.

Large wet antiseptic packs were ordered, to cover all the gangrenous parts on the knees, legs and feet.[7] The temperature then came down quite promptly. These packs were put on for forty-eight hours and then removed, to be replaced as soon as the temperature began to rise again. The patient was now eating well and on the tenth day sat up in a chair. Except for the pain in her feet, she complained very little. The purpuric spots on the arms, hands and upper part of the body faded gradually, leaving small, purplish spots. Over a period of several days the necrotic areas were cut away from the centers of many of the large ulcers. The antiseptic packs were kept on at intervals to prevent extension of the infection and gangrene. With the aid of these packs we could safely wait for a definite line of demarcation so that nothing but the necrotic tissue need be cut away. Penicillin and sulfaguanidine were discontinued on the eighth day after the patient had entered the hospital. One month later she was taken to the operating room and given spinal anesthesia, and the following toes and fragments of toes were removed: the great toe on the right foot, including the distal end of the metatarsal bone; the distal phalanges of the fourth and fifth toes of the right foot; the great toe of the left foot except the proximal phalanx, and all of the third and fourth toes of the left foot. The wounds were all closed fairly tight and healed with but little further removal of tissue. Two weeks later the patient walked with a pair of improvised shoes. At the end of four weeks following the operation she drove her car to the office. The general condition of the patient is good and she walks with very little impairment in her gait.

CONCLUSION

It is impossible to state definitely that any case presents all of the symptom complex of the Waterhouse-Friderichsen syndrome of meningococcic type unless an autopsy is made. The external signs and symptoms seem to place this case in this class. The administration of penicillin perhaps accounts for the favorable result.

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7. Hayes, J. M.: Treatment of Acute Infections of the Extremities, Minnesota Med. **16:** 225-227 (April) 1933.

FATAL AGRANULOCYTOSIS RESULTING FROM THIOURACIL

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The use of thiouracil in the treatment of hyperthyroidism has become widespread. It therefore seems timely to point out that the drug is not completely free from harmful effects. Notable among the complications occurring during the course of thiouracil therapy is agranulocytosis. This may have its onset without any warning and end fatally. Himsworth[1] reported 1 fatal case of agranulocytosis occurring during thiouracil treatment. Details, however, are lacking in this case as to the total dosage and duration of treatment. Astwood[2] reported another fatal case of agranulocytosis. His patient was a man aged 37 with a classic picture of hyperthyroidism. He had received 0.2 Gm. of thiouracil five times a day for twenty-seven days and then 0.4 Gm. five times a day for six days. On the thirty-fifth day he was discharged from the hospital only to be readmitted two days later with severe pharyngitis and a temperature of 103 F. The white blood cell count was 1,100, and no granulocytes were present. Despite intensive treatment with sulfathiazole, liver extract and pentnucleotide the patient died seven days later. Kahn and Stock[3] more recently reported still another case of agranulocytic death of a diabetic patient following the use of thiouracil. Their patient received a total dosage of 30.8 Gm. over a fifty-four day period. At this point the white blood cell count dropped to 1,100, with the appearance of a rash and a pharyngitis. Again despite intensive treatment with transfusions, liver extract and penicillin the patient died in a diabetic coma within five days after the onset of the symptoms. Palmer[4] in a study of 12 thiouracil treated cases observed the depression in the white blood cell count in 2 cases without a change in the differential count. In these 2 cases the white blood cell count returned to normal within three days after discontinuance of the drug. Williams,[5] in a recent review of 125 cases, observed agranulocytosis in 2 cases; no details are given. In a previous report Williams and Clute[6] observed 1 case of agranulocytosis in which recovery followed treatment with large doses of pentnucleotides and liver extract. Bartells,[7] however, in a series of 11 cases noted no untoward effects during the course of the treatment.

Our purpose in this paper is to report an additional case of agranulocytosis following the use of thiouracil, with necropsy.

REPORT OF CASE

History.—A man aged 70, Czechoslovakian, an artist, had fifteen hospital admissions over the past twelve years. Most of these admissions are irrelevant to the present story. Several years before the present admission he had been noted to have an elevated basal metabolic rate and an x-ray shadow in the superior mediastinum interpreted as a substernal thyroid. Because of the age of the patient and the technical difficulties involved, surgical removal of the thyroid was not considered feasible. He was admitted for the fourteenth time Jan. 16, 1944. The chief complaint was weakness and extreme fatigue. The history revealed that he had lost a considerable amount of weight in spite of a good appetite. In addition, he had been suffering from persistent diarrhea and for a few days prior to admission had a productive cough and moderate chest pain.

At that time the patient was extremely emaciated and chronically ill. He was slightly orthopneic and perspired freely. There was a fine tremor of the hands. The thyroid was not palpable. The heart was enlarged to the left, with a systolic

From the First (Columbia University) Medical Division, Bellevue Hospital.

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2. Astwood, E. B.: Treatment of Hyperthyroidism with Thiourea and Thiouracil, J. A. M. A. **122:** 78 (May 8) 1943.
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7. Bartells, E. C.: Thiouracil in Severe Hyperthyroidism, J. A. M. A. **125:** 24 (May 6) 1944.

murmur at the apex. Auricular fibrillation without pulse deficit was present. Scattered rhonchi were heard throughout the lungs. The remainder of the physical examination was entirely negative. The diagnosis of hyperthyroidism was made.

The patient weighed 97 pounds (44 Kg.) on admission. He was given a fifteen day trial of iodine without response. Diarrhea and weakness continued. Administration of thiouracil was then begun. The patient received 0.2 Gm. of the drug four times a day for the first three days. The dose was then increased to 0.3 Gm. four times a day. The latter dosage was maintained throughout the patient's hospital stay. During the first five days of treatment the white blood cell count fell from 9,500 with 60 per cent polymorphonuclear leukocytes to 5,150 with 65 per cent polymorphonuclear leukocytes. During the next thirteen week period the patient gained 31 pounds (14 Kg.). All gastrointestinal symptoms had disappeared. His basal metabolic rate dropped from plus 40 to plus 2. The pulse rate dropped from an average of 100 to an average of 80. The tremor disappeared. His weight of 97 pounds on admission rose to 124 pounds (56 Kg.). The white blood cell count during this period ranged from 5,100 to 7,400. He was then placed on a maintenance dose of 0.9 Gm. daily of thiouracil and discharged to the outpatient department on the one hundred and thirty-first hospital day.

He was followed in the clinic from May 29 until July 3, 1944. During this time he remained asymptomatic and maintained his weight at 124 pounds. In general his health had been excellent and he was completely free from infection. He was kept on 0.9 Gm. of thiouracil once a day for twenty-nine days. Then the dosage was cut to 0.6 Gm. daily for seven days. On July 3 a white blood cell count was taken and was found to be 1,250, with 37 per cent polymorphonuclear leukocytes. He was immediately admitted to the hospital.

The patient felt well for the first two days. His temperature then began to rise and on the fourth day was elevated to 105 F. On the fifth day he was noted to have an inflamed pharynx. The temperature continued to be elevated and his pharyngitis progressed in severity. He died on the seventh hospital day. During this period the white blood cell count continued to fall and was 450 without any granulocytic cells on the day of death. Pentnucleotide given intramuscularly and blood transfusions were of no avail. He had received 113.6 Gm. in one hundred and twenty-eight days.

It should be noted that following the transfusion his temperature became elevated. Penicillin was administered during the last twenty-four hours without any effect on the temperature or course.

Postmortem Examination (performed forty-eight hours after death).—The pharynx was intensely congested and reddened. The thyroid had a normally situated left lobe which was slightly smaller than normal. The isthmus was unchanged. The right lobe was found to be entirely within the apex of the right chest and compressed the apex of the lung downward. It was five times the usual size and coarsely nodular, with the nodules ranging in size from 2 to 4 cm. in diameter. Some of these nodules contained calcium and bone formation, while others were hemorrhagic and necrotic. Large follicles of colloid were visible on section. The trachea was not compressed. The left lobe had a smooth surface. On section it presented a fine, honeycombed appearance. The heart weighed 400 Gm., and all its chambers were dilated. The valves were unchanged, and the ventricular walls were not hypertrophied. The coronary arteries contained a few atheromatous plaques. The lungs showed patchy areas of hemorrhagic consolidation, particularly in the lower lobes. The bone marrow (vertebral and ribs) appeared unchanged. There were no other gross abnormalities.

Microscopic Examination.—The right lobe of the thyroid contained numerous adenomas. For the most part the follicles were filled with colloid; however, the lining of these follicles consisted of low cuboidal cells. An occasional focus was devoid of colloid, and the lining cells appeared to be somewhat more hyperplastic. There was considerable fibrosis present. The left lobe showed nothing unusual. The bone marrow, both with hematoxylin and giemsa preparations, showed moderate hypoplasia of the granulocytic cells. There was definite decrease in the percentage of mature polymorphonuclear leukocytes. The kidneys contained hemoglobin casts in the collecting tubules. In the lungs were patchy areas in which the alveoli were filled with red blood cells and an occasional lymphocyte. In the center of a few of these areas necrosis was present along with numerous bacterial colonies. The anatomic diagnosis was adenomas of the thyroid, agranulocytosis, hemoglobin nephrosis, dilatation of the heart and hemorrhagic lobular pneumonia.

COMMENT

The dosage given in this case is somewhat higher than that which is generally used at present. It was problematic, however, whether the total dosage was related to the onset of the agranulocytosis. It is thought that this complication occurs on the basis of developing sensitivity or idiosyncrasy rather than on the cumulative effect of the drug. In relation to this, Williams,[8] in an analysis of 2 cases treated with thiouracil, in 1 of which death occurred of cerebral hemorrhage and in the other of bronchopneumonia, found that the highest concentration of the drug was in the adrenals, pituitary and bone marrow.

Another finding of interest in this case was the hemoglobin casts in the renal tubules. The patient, however, had several transfusions with rather characteristic transfusion reactions, so that this anatomic change may be accounted for entirely on this basis. However, renal complications with the use of thiouracil have been reported. Palmer [4] reported hematuria without the presence of casts in 1 case, while Williams [6] reported 6 cases in which edema and albuminuria developed. These signs cleared after cessation of therapy. Since this drug is closely related to the sulfonamides and since it is soluble at a p_H of 8.5, it has been suggested that if the renal complications tend to become severe or increase it might be advisable to administer sodium bicarbonate along with the thiouracil. Other toxic manifestations, such as skin eruptions or jaundice, were not noted in this case.

400 East Twenty-Ninth Street.

BILATERAL TEMPORAL ARTERITIS WITH COMPLETE LOSS OF VISION

EDWARD W. SHANNON, M.D., CLEVELAND, AND
JAMES SOLOMON, M.D., BOSTON

Since the original paper of Horton, Magath and Brown [1] many cases of temporal arteritis have been reported, and this syndrome is now recognized as a definite clinical entity.

Temporal arteritis is a self-limited, nonfatal disease characterized by headaches more or less constant and frequently worse at night, general malaise, lassitude, weakness, night sweats and low grade fever, and frequently there is pain in the jaws which makes chewing difficult. The temperature ranges from 98 to 103 F., and the blood may show a mild leukocytosis and an anemia. Mental symptoms are not common, but in a case reported by Sprague [2] there was definite dulling of the intellect. Most of these patients have rather severe constitutional symptoms and appear much sicker than the objective signs would indicate. In the typical case, a few weeks after the onset of the headache, the temporal arteries become tortuous, enlarged and very prominent. Frequently nodules appear along the arteries, which are tender. As the periarteritis progresses, the arteries become thrombosed and all pulsation stops. The occipital arteries are sometimes involved.[3] The fact that the muscle and joint symptoms as well as the constitutional symptoms are so extensive suggests that arteries other than those of the head are involved.[4]

All of the case reports thus far published have been of persons over 50 years of age. There is no significant predilection for either sex.

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8. Williams, R. H., quoted by Palmer, V.: Bull. School of Med., Univ. of Maryland **28**: 125 (Jan.) 1944.

Dr. Shannon was resident in neurosurgery and Dr. Solomon resident in neurology, Massachusetts General Hospital.

1. Horton, B. T.; Magath, T. B., and Brown, G. E.: An Undescribed Form of Arteritis of the Temporal Vessels, Proc. Staff Meet., Mayo Clin. **7**: 700-701, 1932.
2. Sprague, P. H., and MacKenzie, W. C.: A Case of Temporal Arteritis, Canad. M. A. J. **43**: 562-564, 1940.
3. Bowers, J. M.: Arteritis of the Temporal Vessels, Arch. Int. Med. **66**: 384-392 (Aug.) 1940.
4. Dick, G. F., and Freeman, G.: Temporal Arteritis, J. A. M. A. **114**: 645-647 (Feb. 24) 1940.

As in every disease in which the etiologic agent is not known, many theories are presented. The presence of fever and leukocytosis as well as the microscopic appearance of the involved arteries strongly suggests an infectious process. Horton, Magath and Brown [5] carried out bacteriologic studies on the segments of arteries which had been resected. Actinomyces grew from

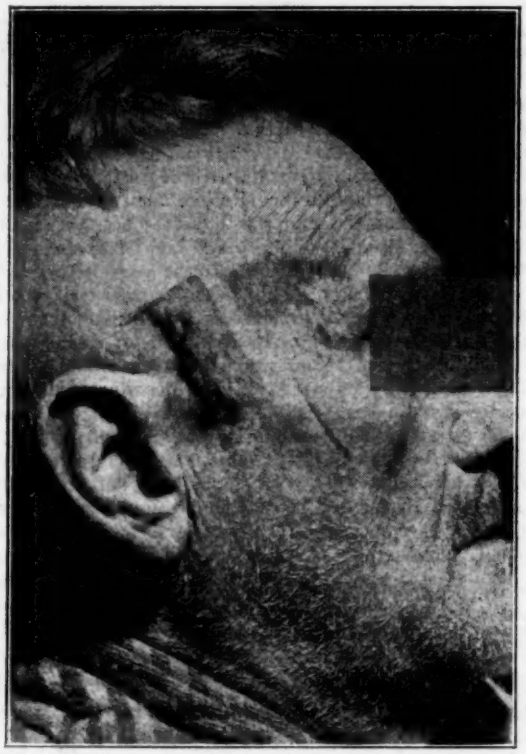

Fig. 1.—Right profile view showing area from which thrombosed temporal artery was removed. The picture was taken several days postoperatively.

these cultures, but they did not feel that the study was conclusive and it has not been confirmed by other investigators. Horton's group later stated that the cause of the disease is not known and suggested that the disease "may be one of the fruits of senility." [6]

The disease is self limited, and no fatalities have been reported. There is no specific treatment for the disease. The most common treatment is resection of a small portion of the involved temporal artery. This usually relieves the headaches, but the constitutional signs and symptoms persist.[7] Bowers [3] combined the injection of large doses of vitamin B_1 with resection of the temporal artery and obtained a good result. It is thought that the relief of the headaches may be due to an interruption of the sympathetic fibers in the temporal artery. However, in the case reported by Sprague and MacKenzie [2] there was no improvement following resection of the temporal artery. Horton and Magath suggested that the persistence of headaches may be due to the deeper cerebral arteries being involved. Schaefer and Sanders [8] reported a case of temporal arteritis in a white woman aged 62 who had very severe constitutional signs and symptoms. She was treated on a Sanders' oscillating bed and cleared up completely. They felt that this treatment was justified, as certain peripheral vascular diseases are treated successfully in the same way. Bain [9] reported a case which completely cleared without surgery or specific treatment. The duration of the disease extends over several months, and the patients make good clinical recoveries, with the exception noted, regardless of what form of treatment is used. Resection of the temporal artery is probably justified in that it is a minor procedure and gives relief from the headaches in a majority of the cases.

The pathologic picture of the involved arteries is characteristic. The lumen is occluded by either cellular or acellular thrombi. There is an infiltration of round cells in the adventitia and vasa vasorum. In some areas of the media there are hemorrhages. The intima is thickened and the basal portion acellular with superimposed cellular layers, which indicates that the intimal proliferation takes place in different stages. Where the media has been destroyed, it has been replaced by a type of granulation tissue in which numerous giant cells are present. The large number of giant cells is the most characteristic feature.[6]

Involvement of the retinal arteries is not a common complication of temporal arteritis, but it does occur and causes either pronounced reduction or complete loss of vision. Johnson, Hurley and Horton [10] report 3 cases of temporal arteritis in which vision was lost. This loss was permanent. These same men quote an unpublished case of R. H. Johnson in which loss of vision occurred in one eye. Dick [4] and Jennings [11] have published reports of cases of temporal arteritis in which there was visual disturbance. It is thought that visual disturbance is secondary to damage of the retinal vessels by the same inflammatory process which involves the temporal arteries. In one of the series reported [10] the visible evidence in the fundi was not sufficient to account for the visual loss. Here it was assumed that occlusion of the vessels had occurred too far back in the optic pathways to produce visible lesions in the retina. Jennings,

Fig. 2.—Left profile view showing tortuous enlarged temporal artery. In addition the emaciation described can be seen.

however, concluded that a distinction between temporal arteritis and periarteritis nodosa is not possible in clinical evidence and is difficult on pathologic grounds.

5. Horton, B. T.; Magath, T. B., and Brown, G. E.: Arteritis of the Temporal Vessels, Arch. Int. Med. **53**: 400-409 (March) 1934.
6. Horton, B. T., and Magath, T. B.: Arteritis of the Temporal Vessels, Proc. Staff Meet., Mayo Clin. **12**: 548-553, 1937.
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8. Schaefer, C. L., and Sanders, C. E.: Temporal Arteritis, Am. Heart J. **24**: 410-411, 1942.
9. Bain, C. W. C.: Arteritis of the Temporal Arteries, Lancet **1**: 517, 1938.
10. Johnson, R. H.; Hurley, R. D., and Horton, B. T.: Arteritis of the Temporal Vessels Associated with Loss of Vision, Am. J. Ophth. **26**: 147-150, 1943.
11. Jennings, G. H.: Arteritis of the Temporal Vessels, Lancet **1**: 424-428, 1938.

REPORT OF CASE

History.—R. M., a white man aged 73, single, a chef, entered the Massachusetts General Hospital in May 1944 because of severe headache and loss of vision. Three weeks before admission he noted the onset of severe pains in his jaws. He thought his false teeth were the cause, but his dentist said they were not. Later he visited a rhinologist, who washed out his antrums on several occasions. The patient, however, had no relief from his pain. In fact, the pain spread and involved his forehead and the back of his neck. The temporal areas became tender. Two weeks before admission the vision in the left eye became blurred and was entirely gone within three days. One week before entry the vision in the right eye became blurred and was entirely gone within two days. (Prior to the present illness he could read fine print with either eye.)

Six months previously he had had "bronchopneumonia," from which he recovered in one week. Other than that his past medical history was not significant. His habits included three to four whiskies and a package of cigarets daily.

The patient was thin and emaciated, with evidence of weight loss. There was no fever. The right temporal artery was tender, reddened and edematous. It had no pulsation in its entire length. The left temporal artery was thickened and tender but pulsated. The arteries in the occipital area were tender, but pulsations were present.

The vision in both eyes was reduced to questionable light perception. There was a pronounced arcus senilis. The pupils were equal (3 mm.) but fixed to light. The view of the fundi was somewhat obscured by the presence of lenticular opacities. They showed venous engorgement, blurred disk margins, papillary and retinal edema, threadlike arteries and some minute hemorrhages. There was some limitation of upward gaze. The ocular tension was 19 in the right eye and 17 in the left eye. There was some tenderness of the eyeballs, with pain when he looked downward. He complained also of a "sticking pain" in the lateral part of the right eye. The vascular system revealed a blood pressure of 150/90 and beaded sclerotic radial arteries. The chest was emphysematous, and expiration was prolonged. The abdomen was normal. The deep tendon reflexes were active but equal, and the plantar responses were normal. Strength in the extremities was good. There were no paresthesias.

Laboratory studies showed an essentially negative urine on two occasions, a red blood cell count of 4,250,000 with a hemoglobin of 90 per cent, and a white blood cell count of 7,750. The differential count on the blood smear was 65 per cent polymorphonuclears, 4 per cent large lymphocytes, 17 small lymphocytes, 11 per cent monocytes and 3 per cent eosinophils. The corrected sedimentation rate was 1.7 mm. per minute. X-rays revealed a chronic right pansinusitis.

Course.—Four days after entry, under local anesthesia, a segment of the right temporal artery was removed. This artery was grossly thrombosed. On microscopic section [12] a granulomatous lesion was seen involving all coats of the artery. The lumen was filled with thrombus (fig. 3) showing evidence of early organization. The wall, but primarily the media, was infiltrated with round cells, polymorphonuclear leukocytes and cells of epitheloid type with scattered foreign body giant cells. The intima was irregularly thickened and involved in the granulomatous reaction; in these areas the elastic lamina was disrupted. The adventitia showed diffuse cellular infiltration together with several well defined granulomas. These consisted of epitheloid cells with a diffuse scattering of polymorphonuclear leukocytes, lymphocytes and a few eosinophils. Numerous giant cells were present, and there was no evidence of central necrosis.

On the day following the operation the patient was completely relieved of headache. However, several days later he complained of a throbbing pain in the forehead and vertex. There was again the sharp shooting pain in the right eye.

Two weeks after entry he was discharged to a nursing home very much relieved of the pain in his head but unable to see.

He was seen three weeks after his discharge and was almost entirely free from headache. Only occasionally was there a twinge of pain in the roof of the right eye and anterior part of each ear. His jaws, which were formerly hard to open, could be opened easily. The vision in both eyes was gone, even light perception. He was in excellent spirits. He said he was not eating well.

On his last visit to the clinic, seven weeks after discharge from the hospital, he was still emaciated but his appetite was improved. The left superficial temporal artery was cordlike and had no pulsation. Vision was entirely gone.

12. Dr. David G. Freiman of the Pathology Department of the Massachusetts General Hospital described the specimen of artery.

SUMMARY AND COMMENT

In a case of bilateral temporal arteritis with complete loss of vision in both eyes, a section of one of the temporal arteries revealed the characteristic picture as described by Horton.[1] The cause of the visual loss is not known, primarily because there had been no autopsies in any of the cases of temporal arteritis. It has been suggested [2] that the retinal artery is the site of a pathologic process similar to that described in the temporal artery. One investigator has actually worked out an anastomosis between the temporal artery and the retinal artery. Other theories have been advanced as well.

Council on Foods and Nutrition

ACCEPTED FOODS

The following additional foods have been accepted as conforming to the Rules of the Council on Foods and Nutrition of the American Medical Association for admission to Accepted Foods.

GEORGE K. ANDERSON, M.D., *Secretary.*

FOODS FOR SPECIAL DIETETIC PURPOSES (*See* Accepted Foods, 1939, p. 295).

The Chicago Dietetic Supply House, Inc.

CELLU BRAND WATER PACKED FRUIT COCKTAIL, consisting of fresh or water packed peaches, pears, Thompson seedless grapes, pineapple and artificially colored and flavored cherries.

Analysis (submitted by manufacturer).—Moisture 91.2%, invert sugar 6.1%, sucrose 0.4%, crude fiber 0.4%, undetermined carbohydrates, etc. (by difference) 0.5%, fat (ether extract) 0.8%, protein (N × 6.25) 0.3%, ash 0.2%.

Calories.—0.36 per gram; 10.22 per ounce.

PREPARATIONS USED IN THE FEEDING OF INFANTS (*See* Accepted Foods, 1939, p. 156).

A. E. Staley Manufacturing Company, Decatur, Ill.

SWEETOSE SPECIAL CORN SYRUP FOR INFANT FEEDING.

Analysis (submitted by manufacturer).—Moisture 25.2%, mineral matter 0.2%, fat 0.0%, dextrose 28.0%, maltose 25.5%, higher sugars 12.0%, dextrins 9.0%.

Calories.—3.06 per gram; 120 per fluidounce.

Beech-Nut Packing Company, Canajoharie, N. Y.

BEECH-NUT STRAINED TOMATOES WITH MILK AND FARINA, consisting of tomato purée, whole milk, water, farina, sugar and salt.

Analysis (submitted by manufacturer).—Total solids 20.7%, moisture (by difference) 79.3%, ash 1.2%, fat (ether extract) 1.5%, protein (N × 6.25) 2.9%, crude fiber 0.4%, Carbohydrates other than crude fiber (by difference) 14.6%, calcium (Ca) 0.07%, phosphorus(P) 0.07%, iron (total) 0.62 mg. per hundred grams, iron(Fe) (available) 0.61 mg. per hundred grams, copper (Cu) 0.20 mg. per hundred grams.

Calories.—0.84 per gram; 24 per ounce.

Vitamins.—Vitamin A.....1,520 U. S. P. units per hundred grams
Thiamine .....0.03 mg. per hundred grams
Riboflavin .....0.20 mg. per hundred grams
Niacin .....0.43 mg. per hundred grams
Ascorbic acid.....2.80 mg. per hundred grams

Gerber Products Company, Fremont, Mich.

GERBER'S STRAINED VEGETABLES AND LAMB WITH BARLEY.

Analysis (submitted by manufacturer).—Moisture 88.6%, ash 1.1%, fat 1.3%, protein (N × 6.25) 2.0%, crude fiber 0.3%, carbohydrates (by difference) 6.75%, calcium 0.014%, phosphorus 0.045%, iron 0.00148%, copper 0.00009%.

Calories.—0.46 per gram; 13 per ounce.

Vitamins.—Carotene, 1.67 mg. per hundred grams.
Thiamine, 0.021 mg. per hundred grams.
Ascorbic acid, 2.42 mg. per hundred grams.

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SATURDAY, MARCH 17, 1945

COORDINATED RESEARCH FOR THE TESTING OF ANTIMALARIAL DRUGS

To the list of volunteers who have aided the advancement of medical science may now be added prisoners in three American penitentiaries. Civilian investigators, aided by grants of funds from the Committee on Medical Research of the Office of Scientific Research and Development, and members of the Army, Navy and Public Health Service have participated in the program. Since March 1944 over 100 prisoner volunteers in a United States penitentiary have been exposed to relapsing vivax malaria in final tests of potential antimalarial drugs prior to their use in the armed forces. Over 100 more volunteers in two other prisons have taken large doses of new drugs for long periods of time to determine whether or not the drugs may safely be used in the prevention and treatment of malaria. The three institutions in which the cooperation of the prisoners has made possible the continuing success of this most important link in the chain of studies to discover a medicinal agent more effective than any now in use against malaria are the United States Penitentiary at Atlanta, Ga., the Illinois State Penitentiary, Stateville, Joliet, and the New Jersey Reformatory, Rahway. In all three penitentiaries the officials and the custodial staffs have cooperated fully.

Quinine and atabrine are efficacious in suppressing the clinical attacks of vivax (benign tertian) malaria, but neither is capable of eradicating the disease completely. Early in 1941 an integrated and comprehensive program of research was organized by the National Research Council and supported by the federal government through the Committee on Medical Research of the Office of Scientific Research and Development. Later the entire program was integrated under the Board for the Coordination of Malarial Studies, a joint body composed of representatives from the Army, Navy, Public Health Service, Office of Scientific Research and Development and the National Research Council. Acting under the board are four subcommittees—the Panel on Synthesis, the Panel on Biochemistry, the Panel on Pharmacology and the Panel on Clinical Testing—which direct the research on malaria and on the development of new antimalarials. The Panel on Biochemistry comprises a group of investigators who are studying the fundamental relationships between the parasite and the cells of the host which it infects. It is concerned also with the mechanism of action of antimalarials on the various developmental stages of the parasite. The Panel on Synthesis supervises the work of chemist-contractors and cooperating pharmaceutic companies engaged in the synthesis of chemicals which are to be tested for antimalarial action. When a drug appears promising, the entire group to which it belongs is fully studied, all chemically related compounds being tested in several avian species. The Panel on Pharmacology supervises the testing of drugs for antimalarial action in animals. These drugs are first tested on chickens, ducks, canaries and turkeys artificially inoculated with their respective species of malaria parasites. Drugs which show promise in these lower animals are then tested, when practicable, on monkeys artificially infected with the species to which these animals are susceptible. Although drugs found to exert antimalarial activity in animals do not necessarily show the same degree of activity in human beings, the vastness of the program necessitates this type of screening in lower animals. This panel also directs studies of acute and chronic toxicity in animals. The Panel on Clinical Testing receives the drugs which have shown promise against malaria in lower animals and monkeys and determines their effect in man.

Chemists have been brought together to synthesize the potential antimalarials: parasitologists to test these compounds against the malarias of birds and monkeys, pharmacologists to determine the relative safety of the effective drugs in higher animals and man, biochemists to develop methods for measuring the amounts of a drug dissolved in the blood and deposited in the tissues of the body and to study the chemical relationship between parasite and host, and finally physicians to put the drugs to critical tests against malaria in man.

The first trial of a promising drug in man is usually carried out against malaria used for the treatment of syphilis of the central nervous system. The malaria is given to the syphilitic by the transfusion of blood containing the parasites, not by mosquito bites, and is treated with the new drug at small, relatively safe doses. Malaria induced by blood transfusion does not relapse; therefore, if a new drug is successful in these preliminary trials, it must be tested against malaria induced by mosquito bite. In order to accomplish this under controlled conditions which will establish beyond question the

effectiveness of the new compound, the drug is tried on normal men willing to contract malaria through the bites of infected mosquitoes and willing to endure the risks associated with taking large amounts of relatively unknown and possibly dangerous drugs.

The three penitentiaries have supplied the testing ground and the human volunteers for such definitive clinical tests of the safety of new drugs and of their effectiveness against malaria acquired by mosquito bite. The immediate direction and supervision of this testing program has been the task of a field laboratory of the National Institute of Health of the U. S. Public Health Service at Atlanta, of the Department of Medicine of the University of Chicago at Stateville, and of the Departments of Medicine and Pharmacology of New York University Medical School at Rahway. All three projects are being carried out under contracts with the Office of Scientific Research and Development.

A prison is an ideal proving ground. Here, in one circumscribed area, live hundreds of men, eating the same meals, working under the same schedules and living the same regimented unvarying existence. To these controlled conditions the medical scientist adds the further safeguards needed to assure the drug a fair and impartial evaluation in its crucial laboratory test. At Atlanta, out of 325 volunteers over 100 have already been infected with malaria and have taken the new drugs that may mean the end of a long and arduous search; at Stateville some 400 prisoners answered the call for volunteers, of whom more than 50 have already started on courses of high doses of new drugs to determine whether or not they may be given safely over long periods; within a month another group of volunteers will receive malaria by the bite of infected mosquitoes and will also receive a new drug in maximum tolerated doses. At Rahway 60 volunteers are deliberately taking increasingly larger doses of several different compounds until the ceiling of safe administration can be established.

When the experiments were begun, the men were fully informed of the objectives of the work, the nature of the disease, the hazards and the inconveniences. A man who volunteered for the experiment was warned to expect malaria—since he surely would develop it were the drug under test not completely preventive in the dosage used. And he was flatly warned that malaria meant that he could anticipate one long siege of trouble for a year and a half or perhaps longer.

By lot, fifteen men draw for positions in the test. Ten of these will begin the drug four days before infection, five will receive enough to test for a possible effect against the earliest hidden forms of the malaria parasites and five will undergo a longer course of treatment to test for a suppressive effect against the clinical attack of malaria which may be expected to appear from six to twenty days after the mosquito bites. The remaining 5 will not receive the drug; these are the controls and must develop malaria to prove that the mosquitoes actually were carriers of infection to the other 10. When clinical malaria has appeared, these controls are used in tests of the curative value of the drug.

The only sure test of infection is finding parasites in the blood; for this the volunteers give a drop of blood from the finger almost daily for months. Serologic tests for the diagnosis of latent malaria are under investigation and chemical tests must be run on blood samples from each man to determine the amount of the test drug circulating in his blood. For these purposes the volunteers submit to the withdrawal of as much as 50 cc. of blood daily for over a week and then at periodic intervals for a month or more. Two weeks after the infecting bites the controls are sick; perhaps a few of the men taking the drug for the short term have also been stricken with malaria. When the men are ill they are given the best possible care in a special unit of the well equipped prison hospital. When the men develop malaria they are treated promptly with large doses of one of the test drugs, and as soon as they are well they return to their jobs in the prison. Periodic observations are continued for months in order to record every instance in which the disease relapses.

Another type of experiment conducted in two of these prisons involves the study of the acute and chronic toxicity of new drugs. Groups of 15 to 30 men each are given daily doses and weekly doses for periods extending over weeks or months. During this time their symptoms are recorded, charted and plotted. They are examined frequently for any gross evidence of toxicity, and the quantity of drug in the plasma is determined frequently. Other tests to evaluate injury to the kidneys, blood, bone marrow and other tissues are instituted.

These experiments have four major functions: (1) to demonstrate the tolerance to the drug of men living under ordinary conditions of activity, (2) to determine whether any latent chronic toxic manifestations result from the prolonged administration of the drug, (3) to determine whether, when given daily or weekly, the drug tends to accumulate in the system or whether excretion keeps pace with administration, and (4) to determine the most satisfactory dosage schedule which will afford a plasma level adequate to protect against vivax malaria.

This research is a demonstration of the manner in which certain projects in the field of medical research are best conducted under governmental auspices. Already medical science has gained vastly; the reports that come from the Bush committee should do much to stimulate a permanent useful mechanism for this type of coordinated research.

PENICILLIN TREATMENT OF VIRUS DISEASES

Experimental confirmation of clinical experience [1] that penicillin is ineffective against virus diseases is reported by Parker and Diefendorf [2] of the Western Reserve University School of Medicine. Equine encephalomyelitis, meningopneumonitis, psittacosis, St. Louis encephalitis and two strains of vaccinia virus were tested by these investigators. Two methods were used to determine viruscidal effects. By the first method the virus was cultivated in Rivers-Li culture medium [3] consisting of a suspension of chick embryonic cells in Tyrode solution, with or without penicillin. After five days' incubation the penicillin containing cultures and the nonpenicillin controls were titrated for virus. By the second method, both virus and penicillin were injected into the yolk sac of intact chick embryos or placed on the chorioallantoic membranes. Development of lesions on the membrane or death of the embryo was taken as a criterion of virus growth.

The results of experiments in which viruses were cultivated in Rivers-Li medium showed that the rates of growth in the presence of 10 Oxford units of penicillin per cubic centimeter within the limits of the experimental error are identical with the rates in the nonpenicillin controls. Similar negative results were obtained in many of the intact chick embryos. In one series of experiments 14 day embryos were inoculated on the chorioallantois with a quantity of vaccinia virus sufficient to give 15 to 50 lesions on each membrane. In the therapeutic tests 500 Oxford units of penicillin was injected into each egg either twenty-four hours before the inoculation or at the time of the inoculation. Differences could not be distinguished between the control and the treated embryos either in the size or number of lesions when the membranes were examined two days later. Negative results were obtained also with St. Louis encephalitis and with equine encephalomyelitis virus.

Distinct therapeutic effects were obtained with meningopneumonitis virus and slight therapeutic results with psittacosis. Of 20 control embryos injected into the yolk sac with meningopneumonitis virus 19 died by the end of the tenth day. In 30 similarly injected embryos treated with 400 Oxford units of penicillin only 6 died by the fourteenth day. Fifty Oxford units gave negative results. With psittacosis virus the 90 per cent control mortality was reduced to 80 per cent by one or more yolk sac injections of 500 to 600 Oxford units.

These positive results are of little clinical interest, since maintenance of a comparable blood concentration of penicillin in man would require the daily injection of several million Oxford units of penicillin. On the whole, Parker's experiments confirm the current clinical belief that penicillin is without practical therapeutic value in virus infections.

1. Indications, Contraindications, Mode of Administration and Dosage for Penicillin, War Production Board (Mimeograph edition), Dec. 1, 1944.
2. Parker, R. F., and Diefendorf, H. W.: Proc. Soc. Exper. Biol. & Med. **57**: 351 (Dec.) 1944.
3. Li, C. P., and Rivers, T. M.: J. Exper. Med. **52**: 465 (Oct.) 1930.

THE HILL-BURTON HOSPITAL CONSTRUCTION BILL

Elsewhere in this issue appear the statements made by two representatives of the American Medical Association before a hearing of the Senate Committee on Education and Labor on the so-called Hill-Burton Hospital Construction Bill. The Board of Trustees of the American Medical Association at a recent meeting indicated that the general policies of this measure are within the platform of the American Medical Association and expressed the opinion that the bill should receive the support of the medical profession.

As was pointed out by Dr. R. L. Sensenich, this measure embraces the principle that the need for an institution is to be established by adequate evidence before funds are allotted for its construction. The Hill-Burton measure recognizes that conditions vary as regards health in different parts of the United States. Obviously the success of this measure, if it becomes effective, will depend largely on the constitution of the Federal Advisory Council, which will have more authority than has generally been granted to such advisory groups in relation to federal agencies. Several suggestions were made by Dr. Sensenich tending toward strengthening of the responsibilities of this council.

As Dr. Sensenich pointed out also the term "public health center" has never been clearly defined. Such an agency might under present definitions undertake a number of functions quite outside the scope of either preventive medicine or the extension of medical service where needed. In certain areas of this country a public health center might be required to undertake procedures which would not be considered either desirable or necessary in other areas.

In his testimony on the Hill-Burton measure Dr. Victor Johnson supplemented the statement of Dr. Sensenich. He emphasized the desirability that a Federal Advisory Council, dealing with the construction of hospitals and health centers, include men of experience in the fields concerned; because of such experience they could command the full support of hospital administrators, physicians and the public.

Dr. Johnson took advantage of the occasion to emphasize again the great importance of legislation which would guarantee for the postwar period adequate numbers of premedical and medical students,

A medical service is no better than the quality of the physicians who render the service. The mere construction of facilities is not in itself any guaranty to an area that it will have sufficient medical care of high

quality. Complete effectiveness in achieving the objective that the proponents of the Hill-Burton measure desire to achieve can come only when construction of facilities is dependent on evidence of ability to maintain the institution and to provide competent personnel.

Current Comment

PENICILLIN AVAILABLE THROUGH NORMAL COMMERICAL CHANNELS

Effective March 15, producers and distributors of penicillin may sell this drug through normal commercial channels. The material will be released in vials containing 100,000 units of sodium penicillin for human parenteral medication. Since May 1944 a limited amount of penicillin has been available for civilian use through the Penicillin Distribution unit in Chicago, which was established by the War Production Board. Hospitals will not be required to place orders through the Penicillin Distribution office, as has been done since last May. However, the office will remain open for a while to meet emergency needs. If a hospital is unable to get penicillin from a distributor it may order from the WPB Chicago Penicillin Distribution office. Distributors have been authorized to sell 1,280,000 packages from March 15 to March 31. An additional quantity of approximately 1,500,000 vials will be made available for distribution in April. Similar quantities are expected to be released each month. Penicillin is not yet in sufficient supply to permit its use in manufactured pharmaceutical products such as pills, lozenges, ointments and other miscellaneous dosage forms. The development and control of penicillin present one of the most important contributions to modern therapy. Cooperation throughout the entire project has been excellent, and all participating members have reason to be proud of their record.

EXPERIMENTAL TRANSMISSION OF RHEUMATIC FEVER

The difficulty in experimental transmission of rheumatic fever has always proved a stumbling block to investigations on that disease. Several years ago Birkhaug [1] reported the self inoculation of a filtrate obtained from a strain of nonhemolytic streptococci isolated repeatedly from a patient with rheumatic fever. About twenty-four hours after the injection acute multiple arthritis developed with fever, pain, swelling and redness. This condition subsided in a few days. Birkhaug's description of the course of events was so striking as to make repetition of the experiment on a larger scale highly desirable. Now Copeman [2] reports the results of some experiments on the transmission of rheumatic fever to a group of adult volunteers. This experiment, like that of Birkhaug, was on a highly restricted basis. It consisted in injecting the blood of a patient suffering with typical rheumatic fever into 5 volunteers. The blood of those who showed any reaction to the initial injection was then taken and injected into a further group of volunteers. Only in the fourth transfer or "generation" of volunteers was there failure to observe reaction of any sort. Of the first group of 5 volunteers receiving blood from a patient with typical rheumatic fever 2 developed mild attacks of rheumatic fever after twenty-four hours. Pain in the shoulder muscles without fever developed three days later in a third volunteer. The blood from the first two volunteers who developed symptoms was pooled on the third day and passed on, producing what appeared to be an attack of fibrositis with fever on the second day in 1 of 4 recipients. The blood of the more severely affected of the first two was again transferred on the seventh day of illness to 4 other volunteers. One of these developed generalized pain (which Copeman calls fibrositis), which six weeks later showed signs of becoming chronic. Finally, the blood of this patient was transferred to 4 recipients on the seventh day after he had himself received a blood inoculation. One of the latter developed mild fever and transitory generalized pain followed in five weeks by a faint apical systolic murmur. Blood taken from this patient on the fifth day, however, did not produce any effect on 4 recipients. Although this group is small and inadequately controlled, as Copeman points out, the results are sufficiently suggestive to warrant extensive and controlled repetition and further investigation, For this purpose monkeys and more particularly human volunteers, who may be available in larger number now than ever before, could well be employed.

1. Birkhaug, K. E.: Rheumatic Fever: Allergic Reactions with a Toxin-Producing Strain of Non-Methemoglobin-Forming Streptococcus Isolated from Rheumatic Fever, J. Infect. Dis. **43**: 280 (Oct.) 1928.
2. Copeman, W. S. C.: Experimental Transmission of Rheumatic Fever, Ann. Rheumatic Dis. **4**: 37 (Dec.) 1944.

ANTEPARTUM PENICILLIN THERAPY

Transmission of penicillin from mother to unborn child through the placental barrier is reported by Greene and Hobby [1] of King's County Hospital, Brooklyn. Four normal patients were tested while in active labor, delivery being expected within two hours. From 20,000 to 100,000 Oxford units of penicillin was injected intravenously into each patient. Samples of maternal blood were taken at the time of delivery, with a sample of placental cord blood as soon as the baby was separated from the placenta. The serum from each blood sample was titrated for penicillin, hemolytic streptococci being used as the test organism. At the time of delivery (thirty minutes to two hours after injection) the amount of penicillin in the maternal blood varied from 0.01 to 0.19 Oxford unit per cubic centimeter, with an average of 0.084 Oxford unit. The average titer of the cord blood was 0.034 Oxford unit, or 40 per cent of that in the maternal circulation. Apparently, then, penicillin passes through the human placenta in sufficient amounts to raise the penicillin titer of the fetal blood stream well above the bacteriostatic level. Practical applications of the implied antepartum penicillin therapy have not yet been suggested.

1. Greene, H. J., and Hobby, G. L.: Proc. Soc. Exper. Biol. & Med. **57**: 282 (Nov.) 1944.

MEDICINE AND THE WAR

ARMY

ANNOUNCEMENT OF QUALIFYING TEST FOR ASTRP

The Sixth Service Command, Chicago, recently announced a nationwide qualifying test for the selection of candidates for the Army Specialized Training Reserve Program which will be conducted on April 12 at all high schools and colleges to which eligible applicants submit requests for the examination. The examination will be administered by a civilian agency which will be responsible for distribution of tests, scoring and reporting results. Complete information will be furnished school officials about March 1. The test will be open to young men who were born after Sept. 30, 1927 and before Sept. 1, 1928 and who will have graduated from high school prior to date of their enrolment in the ASTR Program. Those who qualify on this test will be eligible for enrolment in the ASTR and assignment to selected colleges and universities for terms beginning in the months of July, August and September 1945 only.

To establish eligibility for enrolment in the ASTRP, those who pass the qualifying test are required to enlist in the Enlisted Reserve Corps, but they are not called to active duty until fourteen days after the completion of the term in which they become 18 years of age. Depending on their age at date of entrance into the program, they are eligible for two, three or four twelve-week terms. Trainees accepted for the ASTRP are furnished transportation from their homes to the designated educational institutions, housing, messing, tuition, books, medical care and complete uniforms while in attendance at college. The program may be considered as the equivalent of a government scholarship which effects a saving to parents of about $1,000 in costs of education for the average young man who is eligible for college training for three twelve-week terms.

The course of study in the ASTRP includes mathematics, physics, chemistry, English and history. Those who have completed one or more terms of college will be placed in terms of the course at appropriate levels. A progressive course of physical education is conducted under qualified instructors for six hours a week and the trainees receive five hours a week of basic military training, which is a decided advantage to them when they subsequently are called to active duty and sent to army camps for basic training.

It is desired that the widest publicity be given this program to insure that all school officials, eligible young men and their parents are fully informed of the educational opportunity available to those who can pass the qualifying test on April 12. Applications to take the test should be addressed to high school principals or college registrars and should be submitted as early as practicable. Applications must reach school officials not later than March 31.

REFRESHER COURSES FOR SOME MEDICAL OFFICERS

Major Gen. George F. Lull, Deputy Surgeon General, U. S. Army, recently announced that officers of the Army Medical Department who have been occupied with administrative and other nonprofessional work and who are being assigned duty utilizing their professional skills will have the opportunity of taking courses in their specialties under a new training program just inaugurated. The training will be voluntary and will be open to those members of the Medical Corps who, because of assignment to command, administrative or semiprofessional positions, have not been engaged in the professional side of medical service during the past twelve months or more and whose future military assignments will require professional activity. Every Medical Corps officer of the Army Service Forces returning from overseas assignment will be informed at redistribution stations of this new training program and will be asked to state whether he desires to avail himself of the opportunity. These refresher courses will be given at general hospitals and certain regional hospitals selected by the Surgeon General. Requests for this training will be submitted through channels to the Surgeon General, who will make assignments to hospitals. Officers selected for these courses will go on temporary duty for a period of not more than twelve weeks.

SANITATION COURSE

Twenty-five Hospital Corps officers were selected and ordered to report to the medical officer in command, Medical Research Unit No. 1, Berkeley, Calif., January 1, for temporary duty under instruction in practical sanitation at the University of California for a period of three months. The first two months of the course will be devoted to intensive instruction in the various phases of sanitation. The last month will be utilized for practical field training in sanitation, and on successful completion of the course the officers will be ordered to various naval activities for duty as sanitary inspectors. A second class for this course of instruction will be convened at the University of California, April 1.

AUTHORIZED BADGE FOR MEDICAL PERSONNEL IN COMBAT

A special badge will be awarded to army medical personnel who serve with combat units under fire. The badge is of silver metal, elliptic, with the Medical Department's insigne, the caduceus, and the Geneva Cross superimposed on a litter surrounded by a wreath of oak leaves, and is to be worn on the left breast above decorations and service ribbons. The regimental commander is authorized to make the award for "satisfactory performance of duty under actual combat conditions."

STATEMENT CONCERNING DISCHARGES HELD ERRONEOUS

Secretary of War Henry L. Stimson recently made it known that the statement attributed to the head of the Veterans Administration that 250,000 soldiers a month will be discharged immediately after the war ends in Europe is both unauthorized and without foundation. The basic elements in the War Department demobilization plan were made public last September 6 and remain unchanged. When hostilities cease in Europe the War Department intends to marshal against the Japanese every soldier and every item of equipment that can be used effectively to speed our final victory.

PRISONER OF WAR

Major Ralph W. Hubbard, formerly of Oklahoma City, who was taken prisoner by the Japanese at the fall of Bataan about two and a half years ago, is believed to be in Cabanatuan, Philippines. Recently a message intercepted in a Japanese propaganda broadcast and forwarded by the United States provost marshal indicates that he has been receiving letters, packages and pictures from his wife and other relatives. Dr. Hubbard graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1932 and entered the service Sept. 27, 1940.

TREAT LUZON INTERNEES

Major Nelson Chestnut, formerly of Springfield, Ill., and now commander of the 607th medical clearing company, stated that there were 145 litter cases among the 2,121 liberated persons from the Los Banos internment camp.

ARMY MEDICAL OFFICERS RESCUED ON LUZON

Twenty-one officers of the Army Medical Department, including thirteen doctors, three medical administrative officers, four dentists and a veterinary officer, were named in the first list of prisoners freed from Camp Cabanatuan on Luzon. The list of those freed from Santo Tomas University, Manila, included sixty-six nurses, a physical therapist and a hospital dietitian. The full list of freed prisoners has not yet been officially released and may contain the names of other medical corps officers in addition to the following:

Col. James W. Duckworth, Gosport, Ind.
Lieut. Col. John Edward Kallus, Caldwell, Texas.
Major Ralph Waldo Hubbard, Oklahoma City.
Major Emil Patrick Reed, Brownsville, Texas.
Major Stephen C. Sitter, Milwaukee.
Capt. Ralph Emerson Hibbs, Oskaloosa, Iowa.
Capt. Charles Joseph Katz, Oak Park, Ill.
Capt. Charles Leasum, Sturgeon Bay, Wis.
Capt. Robert B. Lewis, Cape Elizabeth, Maine.
Capt. Robert Kirkwood Whitely, Palo Alto, Calif.
1st Lieut. Harry Merrill Brown, Cicero, Ind.
1st Lieut. Charles Francis Lewis Jr., Oakland, Calif.
1st Lieut. Merle McNeill Musselman, Ann Arbor, Mich.

CHINESE FLIGHT SURGEON HERE

Col. Joseph Shiang-min Lee, flight surgeon, Chinese army, recently visited the Office of the Surgeon General to confer with officers of the training division. Colonel Lee, who is a member of the faculty of the Chinese Army Medical College, Anshun, China, received his military medical training in this country, graduating as a surgeon from the School of Aviation Medicine, Randolph Field, Texas, in 1933 and graduating from the Medical Field Service School, Carlisle Barracks, Pennsylvania, in 1934. He is now visiting medical department training installations to observe the recent advances which have been made in the military and professional training program of the Medical Department.

ORGANIZING NURSE RECRUITMENT

Major Edith Aynes, chief of the Army Nurse Corps Branch of the Technical Information Division, Office of the Surgeon General, and Miss Evelyn Blewitt, civilian consultant to the Surgeon General on army nurse public relations, have returned to Washington after visiting Dallas, Texas, Los Angeles, San Francisco and Portland, Ore. There they conferred with advertising agencies, army nurse recruiting committees, army hospital superintendents and members of the Procurement and Assignment boards participating in the intensified drive for army nurses. A similar trip to the Middle West is planned for the near future.

ARMY MEDICAL DEPARTMENT PERSONNEL REPATRIATED

The War Department recently announced that seventy-seven officers and enlisted men of the Army Medical Department who have been released by Germany will arrive at Charleston, S. C., aboard a hospital ship some time in March. They are the first "protected personnel" under the Geneva convention to be repatriated in this war. The repatriates, whose kin have been notified of their expected arrival, were reported in good health when the hospital ship left Marseille, France. None will require hospital treatment, the War Department said.

MISCELLANEOUS

SURPLUS MEDICAL AND SURGICAL EQUIPMENT FOR CIVILIAN USE

The U. S. Treasury's Office of Surplus Property recently released surplus medical and surgical equipment and supplies by the armed forces for civilian use. Much of the material offered for sale was manufactured for use in the first world war and is in "new" condition, although shelf worn. Each month the regional offices of surplus property inform tax supported institutions and established firms on their mailing lists of medical and surgical properties available for purchase, through the national catalogue "Surplus Reporter." The catalogue, released on March 3, the fourth issue in the series, lists a wide variety of diagnostic and surgical instruments, laboratory equipment, drugs, supplies and treatment equipment of the type used in surgery, examination and treatment of eye, nose and throat, skin, brain and bone. Among the 500 items offered at this time are small 10 inch plaster of paris shears, hemostatic forceps, 6 inch uterine needles (one-half circle with cutting edge), over 5,000 bistouries, a large quantity of analytic filter paper (not acid washed), 250 mm. and of medium speed, over 4,000 rubber surgical operating cushions and a quantity of medical kits, B. Many of the instruments and supplies are displayed in the "sample rooms" maintained at the regional offices of surplus property, where representatives of the Treasury, selected for their professional knowledge, are on duty to assist potential purchasers. A list of the regional offices of surplus property follows:

Region I—Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont. Mr. J. D. Tompkins, regional director, Procurement Division, U. S. Treasury Department, Park Square Building, Boston 16.

Region II—Pennsylvania, New Jersey, New York. Mr. Frank L. Seymour, regional director, Procurement Division, U. S. Treasury Department, 50 Church Street, New York 7.

Region III—Washington, D. C., Delaware, Maryland, North Carolina, Virginia. Mr. M. P. Shlesinger, regional director, Procurement Division, U. S. Treasury Department, 499 Pennsylvania Avenue N.W., Washington 25, D. C.

Region IV—Indiana, Kentucky, Ohio, West Virginia. Mr. R. D. Schell, regional director, Procurement Division, U. S. Treasury Department, Commercial Arts Building, 704 Race Street, Cincinnati 2.

Region V—Illinois, Michigan, Minnesota, North Dakota, South Dakota, Wisconsin. Mr. F. A. Mapes, regional director, Procurement Division, U. S. Treasury Department, 209 South La Salle Street, Chicago 4.

Region VI—Alabama, Florida, Georgia, Mississippi, South Carolina, Tennessee. Mr. H. E. Harmon, regional director, Procurement Division, U. S. Treasury Department, Belle Isle Building, Atlanta 3, Ga.

Region VII—Arkansas, Louisiana, Oklahoma, Texas. Mr. Hamilton Morton, regional director, Procurement Division, U. S. Treasury Department, 609 Neil P. Anderson Building, Fort Worth 2, Texas.

Region VIII—Iowa, Kansas, Missouri, Nebraska. Mr. Thomas C. Stephens, regional director, Procurement Division, U. S. Treasury Department, 2605 Walnut Street, Kansas City 8, Mo.

Region IX—Colorado, New Mexico, Utah, Wyoming. Mr. Alden W. Pool, regional director, Procurement Division, U. S. Treasury Department, Seventh Floor, Exchange Building, 1030 Fifteenth Street, Denver 2.

Region X—Arizona, California, Nevada. Mr. John F. Hough, regional director, Procurement Division, U. S. Treasury Department, 30 Van Ness Avenue, San Francisco 2.

Region XI—Idaho, Oregon, Montana, Washington. Mr. Orrin C. Bradeen, regional director, Procurement Division, U. S. Treasury Department, 2005 Fifth Avenue, Seattle 1.

Region XII—Puerto Rico. Mr. J. T. Gilmer, regional director, Building F, Munoz Rivera Park, San Juan, Puerto Rico.

Honolulu, Hawaii. Mr. Hugh C. Teanent, Procurement Division representative, U. S. Treasury Department, Iolani Palace, Honolulu 2, Hawaii, T. H.

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

Michigan

Percy Jones and Convalescent Hospital, Battle Creek: Laboratory Technics in Differentiating Medical and Surgical Approaches in Regurgitational Jaundice, Dr. E. L. Tuohy, March 19; Anesthesia, Dr. J. S. Lundy, March 26.

West Virginia

The Recognition of Nutritional Deficiency Diseases, Dr. Richard W. Vilter, March 26.

ORGANIZATION SECTION

THE HILL-BURTON HOSPITAL CONSTRUCTION BILL

Summary of statements made February 28 to the Senate Committee on Education and Labor by Dr. R. L. Sensenich, member of the Board of Trustees of the American Medical Association, and Dr. Victor Johnson, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, on Senate Bill 191 (abstracted in THE JOURNAL, *January 27, p. 231).*

Dr. Sensenich's Statement

On behalf of the American Medical Association, I wish to express my appreciation for this opportunity to appear before you to present the views of the Board of Trustees of the American Medical Association on Senate Bill S. 191. The facilities of the American Medical Association are at your disposal in the efforts to obtain a solution of the problem of providing adequate hospital facilities of a high quality for all the people of this country.

The Board of Trustees of the American Medical Association has given careful consideration to the provisions of the "Hospital Construction Act" in the light of the Platform of the Association. The Board, at a recent meeting, took action to the effect that so far as its general policies are concerned the Hill-Burton bill is within the platform of the American Medical Association; that while there are certain modifications that would better define some of its provisions and render the bill more effective, nevertheless it is the feeling of the Board that the bill in general should receive the support of the American Medical Association. . . .

If I may have your permission I should like to distribute a copy of the Platform of the American Medical Association to each member of the Committee and also to include a copy in the record of these hearings. The authors of the bill, and their advisers, are to be congratulated on the basic soundness of their approach.

The Platform of the American Medical Association with regard to the extension of medical care includes the recommendations that funds allotted by Congress "for the prevention of disease, the promotion of health and the care of the sick" should be based on "local determination of needs and local control of administration."

In this bill there has been full recognition of the fact that conditions relating to health and hospital problems vary tremendously in the different parts of the country. A hospital construction plan for a populous, highly urbanized Eastern state may be utterly unsuited to a sparsely populated state of the Rocky Mountain area. Neither of these may be adaptable to a prosperous corn-hog farm state or an economically ill favored tenant farmer state. The Hill-Burton bill appears to provide a maximum of flexible adaptation to local conditions, with a minimum of undesirable uniformity and regimentation.

Should this bill be enacted into law, its successful operation will depend in large measure on the constitution, competence, wisdom and prerogatives of the Federal Advisory Council. The extent to which there is general approval and support of the objectives of the bill will be determined by these appointments. It might be desirable to consider a rewording of the provisions for these appointments, so that lines 24 and 25 on page 14, and lines 1 and 2 on page 15 might read:

> eight appointed members shall be persons who are representative outstanding authorities in fields pertaining to hospitals, public health and medical care activities, and a majority of them shall be representative authorities in matters relating to the operation of hospitals. The first term of four of the . . .

The role of the Federal Advisory Council and its relationship to the administrative activities of the Surgeon General of the Public Health Service are not entirely clear. The provisions of the bill seem sound in the case of the standards for state surveys of hospital facilities, calling for (page 3, lines 12, 13 and 14) "standards prescribed by the Surgeon General *with the approval* of the Federal Advisory Council" (italics not in bill) and in the provision (page 16, lines 19, 20, 21 and 22) requiring that "all regulations and amendments thereto with respect to grants to states . . . shall be promulgated *only upon recommendation* [italics not in bill] of the Federal Advisory Council. . . ." Another desirable provision is that (page 15, lines 20, 21 and 22) "upon request by three or more members [of the Federal Advisory Council] it shall be the duty of the Surgeon General to call a meeting of the Council."

On the other hand, there are certain provisions of the bill in which the prerogatives and responsibilities of the Federal Advisory Council are less clearly defined. For example, with regard to "Approval of Projects and Payments for Construction" (page 9) the Federal Advisory Council is not mentioned in the statement (lines 16, 17, 18 and 19) "The Surgeon General . . . shall determine whether or not to approve such a project." And again (page 11, lines 21, 22 and 23) it is stated that "the Surgeon General shall from time to time estimate the sum to which each state will be entitled under this section. . . ."

There are other instances elsewhere in the bill in which it is not clear whether the decisions of the Federal Advisory Council are mandatory or merely advisory and whether important decisions may be made by the Surgeon General himself. It would appear sound to vest a maximum of authority in a well selected Advisory Council which will collaborate with the Surgeon General, who in turn is the administrator of the Council's policies.

The definition of the "public health center" (page 13) might well be further clarified. Perhaps lines 6, 7 and 8 should be reworded as follows:

> (*d*) The term "public health center" means a publicly owned facility for the provision of public health services as well as such medical care as state surveys indicate to be absent and needed, including related facilities . . .

Obviously, the exact nature of the "public health centers" cannot be sharply defined in advance, since these represent experimental projects. Presumably they will vary in constitution and function from state to state. Experimentation in the establishment of such units is highly desirable and they should be adjusted to local needs.

It is noted in the bill that while a State Advisory Council is provided under section 612 with reference to the preparation of a state plan, no State Advisory Council is provided in the selection of the specific construction to be undertaken under the state plan with the funds available. It would seem desirable to have the advice of some such body in the determination of what construction shall have priority or what modifications of the plan may be desirable as the construction program progresses.

Although maintenance or administration of hospital facilities by the government is not contemplated in the bill, attention has been called by those familiar with Public Law 137, 77th Congress, referring to schools and hospitals erected with government funds, to the content of section 203 (b) and (c) of that law.

Section 203 (c) reads as follows:

> (*c*) No department or agency of the United States shall exercise any supervision or control over any hospital or other place for the care of the sick (which is not owned and operated by the United States) with respect to which any funds have been or may be expended under this title, nor shall any term or condition of any agreement under this title relating to, or any lease, grant, loan or contribution made under this title to, or on behalf of, any such hospital or place prescribe or affect its administration, personnel or operation.

The authors of the present bill apparently are of the opinion that this point has been adequately covered in the organization provided.

In the consideration of the bill before the committee, the question of government contribution to maintenance was discussed where the location of a facility is determined on the basis of medical needs. In each community there will be those who are unable to pay for hospital care as well as those who are able to pay. The facility is established for all the people.

However, illness differs and provisions for treatment must meet the particular needs. Tuberculosis requires special hospitals, long hospitalization and some measure of isolation. Most tuberculosis hospitals are owned and supported by state or county units of government. County tuberculosis hospitals frequently are reimbursed from state funds at a fixed amount per patient daily.

The care of the insane has long been recognized as the direct responsibility of government.

Chronic illness of other types, especially the slowly progressing illness of the aged, requires long periods of hospitalization, and beds cannot be given over for these patients in hospitals planned for the care of acute illness. No doubt this fact will lead to the eventual establishment of more special hospitals for chronic disease. Some unit of government must support the indigent in these hospitals. State and local governments may be stimulated to accept their full responsibility.

A study of the indigent group reveals a great concentration of chronic incurable disease, the crippled and the mentally inadequate. The number of others who are temporarily medically indigent is relatively small.

The community may need a general hospital that will be practically self supporting if the individual indigent is given assistance by local responsible authorities.

No single plan for financial aid in hospital maintenance would be suitable for the provision of the best medical care for each individual in such widely different categories.

This bill includes under the definition of hospitals public health centers and general, tuberculosis, mental, chronic disease and other types of hospitals and related facilities. It is sufficiently flexible to be useful in whatever portion of the field of hospital care that need is demonstrated. It may, therefore, provide special facilities for many of the varied types of the chronic disease indigent groups.

The American Medical Association is primarily interested in the best medical care for all the people. It would seem inadvisable to attach to this bill any plan for financing maintenance such as would render the bill less flexible and impair its effectiveness in providing facilities for different groups under varying local conditions.

The bill now provides the means for the development of facilities for the best hospital care for all the people on the basis of needs as determined by investigation and by careful planning to meet those needs.

The suggestions for modifying and strengthening this bill do not alter the position of general approval. This bill conforms to the Platform adopted by the House of Delegates of the American Medical Association. It is endorsed by the Board of Trustees of the Association and deserves the support of all members and organizational units of the American Medical Association. Its authors are to be commended on their scientific approach to this important problem.

The American Medical Association stands ready to be of every assistance within its power to the Committee on Education and Labor, or its subcommittee, in further problems related to the Hill-Burton bill and its objectives.

Dr. Johnson's Statement

I appreciate the privilege of appearing before you as a representative of the American Medical Association and its Council on Medical Education and Hospitals. This council has been concerned for over forty years with the maintenance of medical care of a high quality, by fostering and stimulating high standards in the education of the physician. The responsibilities of the Council include rendering the services of consultation, advice and accreditation to medical schools and to hospitals engaged in educational programs at the levels of the internship and residencies in the specialties of medicipe.

In addition, the Council promotes improved care in hospitals not engaged in the teaching of medical students, interns and residents. It maintains a register, now including 6,645 hospitals, as a service and protection to hospitals and the public, since the register includes only those hospitals which have been determined to measure up to certain minimum standards of hospital and medical service.

The Council on Medical Education and Hospitals is glad to offer to this committee and to such state agencies as might be set up under this bill all the detailed information it collects and publishes annually concerning the hospitals of this country.

Primarily, I wish to second the remarks of Dr. Sensenich, whose testimony preceded mine, and who supported the bill under discussion. My remarks are merely supplementary to his. However, I should like to stress the opinion that the composition and powers of the Federal Advisory Council are extremely important. This body should consist of men who will command the full support of hospitals, physicians and the public. I think the council should be more than advisory and that it should be clothed with considerable authority, as seems to be the intent of the bill. Such an arrangement with powers of both veto and the initiation of action by the council is entirely consistent with good and efficient administration. There are numerous examples of such plans in business, industry and the professions.

I am very much impressed, and I think I can speak also for the Council on Medical Education and Hospitals, with the scientific approach manifested in this bill. The only a priori assumption made in this bill is that there is a maldistribution of hospital facilities in various parts of the country, with which assumption all must agree. The manner in which this faulty distribution is to be assessed conforms to the best scientific procedures. The proposed surveys, conducted by states agencies with the assistance of all groups concerned with hospital care, should provide the information requisite for an intelligent program of hospital construction in areas deficient in hospital facilities.

The sound approach to a solution of the problems of better distribution of medical care and hospital facilities on the part of the Committee on Education and Labor is reflected not only in the provisions of this bill but in the approach to these problems by your Subcommittee on Wartime Health and Education, under the chairmanship of Senator Claude Pepper. The interim report of this committee, published in January 1945, is an admirable document, containing invaluable information for the formulation of programs for improved medical care.

Certain of the procedures suggested in this report and in the Hospital Construction Bill are practically identical and equally sound. The report (page 17) recommends that "state programs should be drawn up by state health planning commissions" and "Before federal funds could be granted, however, overall state plans and individual projects should be reviewed and approved by the United States Public Health Service to make sure that they meet certain standards of construction, operation and complete, coordinated service." Equally significant is the recommendation that "grants to both public and voluntary institutions included in the plan would be administered through a state agency."

The provision of hospital and diagnostic services occupies a key position in the more equitable distribution of medical care. The days of the horse and buggy doctor are gone forever. Good medicine can be practiced only when hospital and related diagnostic facilities are available. Physicians may choose to locate in a community providing these facilities even though his income may be less than in areas lacking them. United States Public Health Service studies have shown that in areas of equal per capita income there may be three times as many doctors if hospitals are available as there are if such necessities of modern medical practice are lacking.

Studies conducted by the American Medical Association and by the Committee on Postwar Medical Service indicate that twice as many medical officers returning to civilian practice after the war will be willing to go to areas with deficient medical service if hospital and diagnostic facilities are provided, as compared with those willing to locate in medically deficient areas without such facilities.

If it is true that physicians cannot be attracted to rural and medically deficient areas without provisions for hospital facilities, it is equally true that hospitals without physicians are worthless. I should like to take this opportunity to stress to this committee what I have stated to your subcommittee: The present policies of governmental agencies regarding the supply of medical students is such that we shall be faced with a drastic reduction in the number of physicians after the war. Today the lack of provisions for the training of doctors is such that we may anticipate that many hospitals constructed under this bill, if it is passed, will have no physicians to man them.

In 1944 Army and Navy students entering our medical schools constituted 80 per cent of the entering classes. Twenty per cent were selected from civilian sources. It was becoming increasingly difficult for admissions committees to secure even this small percentage of qualified civilians from the sources available. In the year 1945 only about 53 per cent of the entering students will be Army or Navy students, increasing to 47 per cent the numbers which must be obtained from civilian sources. In 1946 there will be no Army students, and only approximately 10 per cent of the entering freshmen will do so under the Navy auspices. This increases those to be obtained from civilian sources to 90 per cent of the entering classes. One of two consequences is inevitable. Either the students will be of far poorer quality or they will be far fewer in number. We cannot afford either alternative. It will be impossible to obtain these large numbers of students from the category of men under 17, physically disqualified men, veterans and women. At the present time there is an utterly inadequate number of qualified individuals entering premedical training. I appreciate that a number of you are concerned with this problem. Conversations have been held with Senator Pepper regarding solutions to the problem and on Monday of this week Senator Ellender introduced a bill, S. 637, which was referred to the Committee on Military Affairs. This bill would seem to provide adequately for the exigency.

I wish to reiterate my appreciation of the privilege of expressing these views and to repeat that every facility of the Council on Medical Education and Hospitals is available to this committee in its efforts to implement and improve the bill under consideration. Finally, I wish to emphasize the opinion that this hospital construction bill deserves the support of all who are concerned with the extension and improvement of medical care in this country.

Postwar Medical Service

The Joint Committee on Postwar Medical Service met in Chicago on February 10. The meeting was called to order by the Chairman, Dr. Ernest E. Irons, at 10:05 a. m. The following members of the Joint Committee were present: Dr. Irvin Abell, Dr. Arthur W. Allen, Dr. Walter L. Bierring, Dr. Frederick A. Coller, Mr. Graham L. Davis, Capt. William E. Eaton, Dr. Morris Fishbein, Dr. E. L. Henderson, Dr. Ernest E. Irons, Lieut. Col. H. C. Lueth, Dr. James M. Mason, Dr. James E. Paullin, Dr. George Morris Piersol, Brig. Gen. Fred W. Rankin, Rev. A. M. Schwitalla, S.J., Dr. H. H. Shoulders, Dr. LeRoy H. Sloan, Miss Mary Switzer and Dr. Olin West. Also present were Lieut. Col. R. D. Bickel, Lieut. Col. G. R. Gessner, Mr. J. W. Holloway Jr., Dr. Victor Johnson, Dr. Edwin P. Jordan, Col. B. R. Kirklin, Dr. Herman L. Kretschmer, Capt. Stephen J. McDonough Jr., Col. Hugo Mella, Col. F. V. Meriwether and Dr. R. L. Sensenich.

APPROVAL OF MINUTES OF DECEMBER 9, 1944 MEETING

The minutes of the meeting of the Committee held in Chicago on Dec. 9, 1944 were approved as circulated. It was moved by Dr. Abell after discussion by the Chairman that the minutes of the present meeting be circulated among the members of the Committee and a mail vote of approval taken, after which the minutes should be printed in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION in order that the profession at large, including military personnel, might be informed of the progress of the Committee's work. The motion was duly seconded and carried, and it was understood that this would be the procedure to be followed in the future.

COMMITTEE MEMBERSHIP

The Chairman announced that the Board of Trustees of the American Medical Association had not yet had opportunity to appoint any one to represent the Association as a member of the Joint Committee in the place of Dr. Alan Gregg, resigned.

It was announced by the Chairman that Dr. Walter W. Palmer, a member of the Committee representing the American College of Physicians, has presented his resignation because of new and important duties recently assigned to him. The resignation of Dr. Palmer was accepted with regret. The Chairman stated that the American College of Physicians would appoint a successor to Dr. Palmer at an early date.

A communication from Surgeon General Parran requested that Col. F. V. Meriwether represent the U. S. Public Health Service whenever it is not possible for Dr. R. C. Williams or Dr. Warren F. Draper to attend the meetings of the Committee. The request was acceded to.

The Chairman stated that it was expected that the Advisory Board for Medical Specialties would name some one at its meeting to be held on February 11 to represent that organization on the Committee.

PROGRESS REPORT ON THE ANALYSIS OF QUESTIONNAIRES SENT TO MEDICAL OFFICERS

Lieut. Col. H. C. Lueth, Liaison Officer, stated that he had prepared a report which comprised more than fifty-eight typewritten pages and would at the moment present only the highlights, and that he hoped the Committee would approve having the complete report printed in THE JOURNAL.

Following is a brief summarization of Colonel Lueth's extremely informative report:

1. Future educational desires of medical officers on duty with the Army, Navy, Public Health Service and Veterans Administration were determined by a study of 21,029 returned questionnaires.

2. Nearly 60 per cent of the group, 12,534, wanted to take long courses (six months or longer) of further training in hospital or educational work. About one fifth of the group, 4,563, indicated they wished to take short courses (less than six months).

3. There were 3,922 medical officers, or 18.7 per cent of the group, who did not want any future training.

4. Requests for short courses included all specialties. The largest number of requests were for the following specialties in order of frequency: internal medicine, surgery, general review, obstetrics and gynecology, pediatrics, otolaryngology and ophthalmology.

5. The ten most popular special fields of training by means of long courses, in order of frequency of request, were surgery, internal medicine, obstetrics and gynecology, general review, psychiatry and neurology, pediatrics, orthopedic surgery, ophthalmology, radiology and otolaryngology.

6. Nearly two thirds of the group, 13,333, or 63 per cent, expressed a desire to become certified specialists. There were 3,324 medical officers, nearly 16 per cent of the entire group, already certified by the American specialty boards. The remainder either did not care to be certified or did not mention their desires.

7. Nearly 40 per cent, 8,734 medical officers, came from private practice to the military services. Twenty-two per cent, 4,640, came directly from internships; nearly 10 per cent, 2,191, came directly from residencies, and the remainder came from various types of practice. About 15 per cent failed to answer the question concerning their previous type of medical practice.

8. A comparison of the results of a pilot questionnaire and the present questionnaire was made. Long courses were requested by about one fifth more men in the final questionnaire than in the pilot questionnaire. Only two thirds as many men requested short courses in the final questionnaire as in the pilot. The difference was attributed to a change in the point of view of medical officers during the interval between the circulation of the questionnaire rather than to an error in sampling.

The report presented by Col. Lueth was accepted with thanks and commendation, and its publication at the earliest possible time was authorized.

REPORT ON BUREAU OF INFORMATION

Dr. Olin West stated that the Bureau of Information is now functioning but to a limited degree because of the extreme difficulty encountered in getting and keeping personnel. He stated that the Bureau had up to this time completed tabulations for thirty-eight states. Copies of the forms that are being used to secure information for the purposes of the Bureau and of the Instructions for Completing County Summary Sheets were submitted. Dr. West further stated that it was hoped and expected to have the cordial cooperation of the constituent state medical associations and the component county medical societies in the Bureau's effort to collect all pertinent information. He stated that inquiries are coming in from men on active duty but to a larger extent from men who have already been discharged and that he was confident that the Bureau will perform a helpful service. In reply to questions, Dr. West stated that the state medical associations had been informed of the work of the Bureau and many had expressed their willingness to cooperate; that instructions had been forwarded to the county medical societies; that some of the state societies have organized their own plans along these lines and that the Bureau will keep in close contact with all of them.

It was stated by Colonel Lueth that at present the problem is threefold: education, licensure and location. Information on

educational facilities is best handled in one central place, and Dr. Victor Johnson, Secretary of the Council on Medical Education and Hospitals, is attempting to perfect a plan toward this end so that inquiring medical officers can be informed of available opportunities for training. The question of location in specific communities is a local problem, which will be referred to the state agencies under close cooperation with the central file.

It was brought out in the discussion that there is much confusion in the states concerning the selection of hospitals and educational institutions under the provisions of the G. I. bill; that in some states the state department of education is advising the governors—in several states the organization of the work is behind and in others far ahead, and that it will be necessary to "tie up" the hospital, educational and licensing elements into a coordinating group. The Committee on Postwar Medical Service will be able to exercise such a coordinating action.

On motion of Dr. Paullin a committee was appointed to draw up recommendations on these questions. The committee, composed of Dr. Shoulders, Miss Switzer and Dr. Coller, presented the following resolution, which was adopted after discussion in which it was noted that under the G. I. bill the governors of the states are given control over all phases of education of veterans:

Resolved, That the chair be authorized to appoint a subcommittee to

1. Draw up recommendations to the governors of the several states concerning the medical education and postgraduate training of veterans under title II of Public Law No. 346, the Servicemen's Readjustment Act of 1944, with particular reference to the certification of institutions as qualified to give such training, and

2. Coordinate this effort with related medical and health problems in the state.

The Chairman announced the appointment of the subcommittee authorized under the foregoing resolution, as follows, stating that the new subcommittee would be expected to report back to the Joint Committee at its next meeting: Dr. H. H. Shoulders, Chairman, Dr. James E. Paullin, Rev. A. M. Schwitalla and Dr. Frederick A. Coller, with Miss Mary Switzer and Lieut. Col. H. C. Lueth as consultants.

PROGRESS REPORT ON EDUCATIONAL OPPORTUNITIES FOR MEDICAL OFFICERS

Dr. Victor Johnson presented a progress report on educational opportunities for medical officers, stating that it would be necessary to modify some of the estimates of available residencies on the basis of the analysis presented by Colonel Lueth. He stated that developments so far are promising and, if institutions and individuals involved continue with the same vigor and industry, the need will be met. Further reports will be made to the Committee.

During the discussion of Dr. Johnson's report, the question was asked if all of the residencies that would be available are of a type that would lead to certification by specialty boards, and the reply was that many would be second year training and that those hospitals initiating new residencies would have to be considered by the Council on Medical Education and Hospitals and by the specialty boards. This progress report will be continued at the next meeting.

REPORT OF SUBCOMMITTEE TO CONFER WITH THE SURGEONS GENERAL ON EDUCATION OF MEDICAL OFFICERS

(Dr. Coller, Chairman; Dr. Palmer; Father Schwitalla; Dr. Johnson; Lieutenant Colonel Lueth)

Dr. Coller stated that his committee had nothing new to report. Father Schwitalla thought there were other questions the subcommittee might look into, and the subcommittee was continued to follow up such phases as it may consider necessary and report at the next meeting.

PROGRESS REPORT ON ARMY AND NAVY PLANS FOR RESIDENCIES AND GRADUATE STUDY

Capt. William E. Eaton had little to add to the report given at the last meeting when he had informed the Committee that the Surgeon General of the Navy had accepted certain plans for providing refresher courses for naval medical officers. Since then the professional division of the Bureau has been pursuing the classification of naval hospitals for internship and graduate training, and information relative to fellowships and residencies has been sent to officers in command. He stated that an attempt is being made to improve methods of training that have been in effect for many years, and that activity in the whole matter is not yet completed.

Col. G. R. Gessner reported that the Army is readjusting the specialties practiced in its general hospitals and increasing and readjusting the size of the facilities now available. The Surgeon General has deferred any further action until a little firmer basis can be found on which to work before establishing a program of this type in Army hospitals. With the publication of Army Service Forces Circular No. 41 on Feb. 5, 1945 refresher professional training was authorized for officers of the Medical Corps who for the past twelve months or longer have been in administrative or command positions and who it is contemplated would be reassigned to professional duties. This training will be given in hospitals in both medicine and surgery and will be voluntary and available to any officer of the Medical Corps, with priority given to those who have been overseas. Such officers will be ordered to temporary duty to take the course of instruction on their own request and will be continued in active service.

Brig. Gen. Fred W. Rankin stated that the refresher course plan has nothing to do with the specialties, and that the Army has no intention of putting these men into a type of specialized training that would qualify them for specialty board certification.

Col. F. V. Meriwether, representing the Public Health Service, in place of Dr. R. C. Williams, stated that Dr. Williams had written him that in service hospitals there will be places for about thirty residencies, which will be available after the war and that the contemplated expansion may raise the number somewhat. He stated, with reference to education, that the Public Health Service is carrying on a training course in civilian schools for the benefit of Public Health Service officers, both regular and reserve, and that this is a more or less specialized public health training.

The chairman indicated that he would ask for further progress reports from each service at the next meeting.

REPORT OF WAR SERVICE AND POSTWAR PLANNING COMMITTEE OF AMERICAN DENTAL ASSOCIATION

The Chairman presented a statement he had received from Dr. C. Willard Camalier, Chairman of the War Service and Postwar Planning Committee of the American Dental Association, concerning the work of that committee, and stated that the invitation to the American Dental Association to send a representative to future committee meetings would be renewed.

REPORT OF SUBCOMMITTEE ON SURPLUS MEDICAL AND HOSPITAL SUPPLIES

(Dr. Palmer, Chairman; Dr. Irons; Dr. Fishbein; Father Schwitalla; Miss Switzer)

Miss Switzer reported that since the last meeting of the Committee on Postwar Medical Service a Surplus Property Board had been appointed; that the U. S. Public Health Service had drawn up a plan for the disposal of surplus medical supplies, and that Dr. Paul M. Stewart, who had prepared the plan, had sent copies of it to the various professional organizations interested. After discussion, this subcommittee was continued with Father Schwitalla as Chairman in place of Dr. Palmer. Dr. George Morris Piersol was appointed a member of this subcommittee. The subcommittee was instructed to review the plan and to report back to the Joint Committee with recommendations to be presented to the American Medical Association.

LAWS CONCERNING TEMPORARY LICENSURE: PROGRESS REPORT

Dr. Walter L. Bierring reviewed the previous actions of the Committee on Postwar Medical Service in the matter of temporary licensure and stated that the Federation of State Medical Boards was having a meeting within the next two days at which Dr. Paul C. Barton, executive officer of the Procurement and Assignment Service, is to present a discussion of the matter and bring to the attention of the delegates additional facts regarding the need in certain communities. He stated further that at the present time four states—Pennsylvania, Delaware, Nevada and Florida—have adopted statutes

involving temporary licensure; that no measures have been introduced in other state legislatures now in session, and that at the coming meeting of the Federation the attitude of that body toward temporary licensure should be determined. He gave a résumé of a report that Colonel Lueth is to make to the Federation delegates on information with respect to licensure that has been gleaned from the questionnaires sent to medical officers. Dr. Bierring stated that the Federation of State Medical Boards will be glad to do its utmost to bring about an equable and desirable solution of the problem.

Colonel Lueth asked that approval of the Committee be given him to provide Dr. Bierring with the material on licensure obtained from the analysis of the questionnaires. This was granted.

REPORT OF SUBCOMMITTEE TO CONFER AND COOPERATE WITH VETERANS ADMINISTRATION CONCERNING EDUCATIONAL ASSISTANCE FOR VETERANS

(Father Schwitalla, Chairman; Drs. Coller and Palmer)

Father Schwitalla said that his subcommittee had nothing new to report. He stated that one big difficulty being encountered by most of the veterans is the availability of service in hospitals.

REPORT OF SUBCOMMITTEE ON ESTABLISHMENT OF MEDICAL CORPS IN VETERANS ADMINISTRATION

(Father Schwitalla, Chairman; Drs. Shoulders and Sloan)

Father Schwitalla reported that he had held a number of conferences in an effort to familiarize himself with the laws governing the Veterans Administration and the methods by which its medical personnel was being administered under Civil Service. The criticism of the medical care under the Veterans Administration has been increasingly vocal during the last few weeks. Examples were quoted. It was pointed out further that activities were in progress contemplating the reorganization of medical procedures under the Veterans Administration. A further report was promised for the next meeting of this committee.

SOURCES OF FUNDS TO BE USED FOR POSTWAR MEDICAL EDUCATION

Mr. Graham L. Davis informed the committee that the trustees of the W. K. Kellogg Foundation had recently approved a program under which financial assistance would be given over a three year period to a selected group of fifteen medical schools in the development of postgraduate educational opportunities for physicians in the areas they serve and to eight universities interested in establishing courses in hospital administration for both physicians and laymen.

OTHER POSTWAR PROPOSALS

Miss Switzer, who had been requested at the December meeting to gather material on the postwar planning of other organizations, reported that it had been impossible because of the pressure of other duties to go into this matter, and the Chairman stated that it would carry over to the next meeting.

PROGRAMS FOR ENROLMENT OF MEDICAL STUDENTS

Colonel Gessner and Captain Eaton both stated that they would gather information as definite as possible concerning the status of the Army Specialized Training Program and the Navy V-12 Program for presentation by themselves or by someone else more closely connected with these matters at the next meeting of the Committee on Postwar Medical Service.

LETTERS FROM MEDICAL OFFICERS IN SERVICE

The Chairman informed the Committee that letters of complaint that had been received from medical officers had been handled in the manner agreed on by the Committee at its December meeting.

INFORMATIONAL REPORTS

Association of American Medical Colleges.—The Chairman informed the Committee that Dr. Fred C. Zapffe, representing the Association of American Medical Colleges, could not be present but that he expected to attend the next meeting, at which time he would hope to provide the Committee with pertinent information.

Wartime Graduate Medical Meetings.—In the absence of Dr. F. F. Borzell, acting chairman of the Central Committee of the Wartime Graduate Medical Meetings, the Chairman stated that the work is being carried on; that the surgeons general had been appealed to for their aid in continuing the meetings under the wartime transportation restrictions, and that the details of the programs are being published regularly in THE JOURNAL, the *Annals of Internal Medicine* and the *Bulletin of the American College of Surgeons.*

Federation of State Medical Boards.—Dr. Bierring had nothing to report beyond what he had had to say earlier in the meeting with respect to licensure.

American Hospital Association.—Mr. Graham L. Davis stated that one of the major interests of the Hospital Association is Senate Bill 191, the Hospital Construction Act, or, as sometimes called, the Hill-Burton bill; that one of the purposes of the bill is to relocate physicians where they can be of the greatest use, which, as he understood it, was also one of the purposes of the Committee on Postwar Medical Service. He stated that, if it works out, the major part of the funds appropriated will be spent on hospitals in rural areas; that the federal government has a function and a responsibility for distributing the funds on the basis of need; that under the bill the Surgeon General of the U. S. Public Health Service would take into consideration the economic status in the particular area, and that some of the poorer states would receive 75 per cent assistance.

Mr. Davis requested as much support as possible from the American Medical Association toward the passage of the bill. He stated that the Hospital Association was cooperating very closely with the Surgeon General in the matter, and that thirty-three states now have in process studies of hospital needs.

Father Schwitalla informed the Committee that the other hospital associations had collaborated with the American Hospital Association in the preparation of the Hospital Construction Act and gave as points in its favor that while it centralizes responsibility in the hands of the Surgeon General it makes it incumbent on him to consult with his advisers; that the needs of the states are dominant in size of the funds allotted, and that the bill safeguards the relationship between the tax supported hospitals and the private hospitals.

Veterans Administration.—Col. Hugo Mella reported that the Veterans Administration is still working on the development of residencies; that a number of the Veterans hospitals had been surveyed by the American College of Surgeons for that purpose, but that it probably will not be possible to ascertain the complete number of residencies available until after the war. Each station after being surveyed has been asked to build up its plans.

Liaison Office.—Lieutenant Colonel Lueth announced that Lieut. Col. R. D. Bickel had been assigned to the Liaison Office at the American Medical Association headquarters and was now functioning. The Committee expressed its satisfaction at having Colonel Bickel present.

Procurement and Assignment Service.—Dr. James E. Paullin, member of the Directing Board of the Procurement and Assignment Service, stated that the Procurement and Assignment Service has contacted all discharge areas for physicians and is attempting through its state chairmen, to find out when a physician is being discharged and, if he has not already determined on a location, to furnish him with information as to understaffed communities.

CONTINUATION OF SUBCOMMITTEE

Dr. Coller suggested that the subcommittee of which he and Father Schwitalla were now the only members and of which Dr. Palmer had been chairman should be discontinued in favor of the larger subcommittee that had been appointed at this meeting. The Chairman stated that the subcommittee mentioned by Dr. Coller was a standing committee and that the new subcommittee was appointed to do a particular job and would be through when the job is done.

TIME AND PLACE OF NEXT MEETING

The next meeting of the Committee on Postwar Medical Service will be held at American Medical Association Headquarters in Chicago on March 17, 1945.

The meeting adjourned at 1:10 p. m.

H. H. SHOULDERS, M.D., Secretary.

Washington Letter

(From a Special Correspondent)

March 12, 1945.

Medical Science Eliminating Venereal Diseases

Such progress is being made by medical science against venereal disease that within five years syphilis and gonorrhea will be removed from the list of major health problems, according to Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service. In an OWI report Dr. Parran stated that in the last eighteen months penicillin has had a "cure rate" of 96 per cent among all gonorrhea patients and also "cures some cases of infectious syphilis." The report dealt in detail with wartime health and problems to be expected when peace returns. There is no indication of a serious decline in the nation's mental and physical health, but Dr. Parran warned that the "lines against disease are lightly held." Shortages of medical manpower and the shifting population "leave us vulnerable to a breakthrough on many fronts." The shortage of doctors and nurses for civilians was expected to continue until both Germany and Japan are defeated. In the first ten years after the war the country will need 417,000 new hospital beds, including 191,000 for mental patients and 60,000 for the tuberculous. Installations of all the hospital beds and health centers which would be needed would cost almost $2,000,000,000, Dr. Parran estimated. Rural areas would have an urgent need for small, well equipped hospitals and health centers.

Campaign Planned to End Venereal Disease by 1950

The plan to exterminate venereal disease by 1950 has been explained by Army, Navy and Federal Security Agency representatives to law enforcement, health, welfare, trade, industrial and civic officials in three key cities, Oklahoma City, San Antonio, Texas, and Columbia, S. C., Paul V. McNutt, Federal Security Administrator, has announced. Mr. McNutt said the fact that 40 per cent of venereal disease cases reported by the Army and Navy are acquired by enlisted personnel while on furlough indicated the need for a concerted community attack on prostitution, promiscuity and venereal disease. Until recently the venereal disease control program has been centered in war industry areas and cities near military cantonments, but the new developments are said to indicate that the problem is nationwide and not confined to war impacted areas. Mr. McNutt said that adding to the need for a new approach to the problem were recent advances in medical science in treating venereal infections, among which are rapid treatment methods for syphilis and the release of penicillin to civilian physicians for treatment of gonorrhea. Appearing at the three conferences were Thomas Devine, newly appointed director of the Social Protection Division, Office of Community War Services, Federal Security Administration; Mark McCloskey, director of the Office of Community War Services; Lieut. Col. Thomas H. Sternberg, director of the Venereal Disease Control Division, Office of the Surgeon General, War Department; Comdr. W. H. Schwartz, officer in charge of the Venereal Disease Control Section, U. S. Navy, and Dr. J. R. Heller, medical director in charge of the Venereal Disease Division, Public Health Service, Federal Security Administration.

Neuropsychiatric Institute Proposed for Capital

Construction of a $4,500,000 plant in Washington by the Federal Works Administration to house a proposed National Neuropsychiatric Institute is provided in a bill introduced in the House by Representative Priest, Democrat of Tennessee. The institute would be organized under the U. S. Public Health Service "for the purpose of conducting research, investigations, experiments and demonstrations relating to the cause, diagnosis and treatment of neuropsychiatric disorders." It would also make grants in aid to universities, hospitals, laboratories and other public and private institutions and to individuals for research projects recommended by a national advisory mental health council provided in the bill. The Surgeon General of the U. S. Public Health Service would appoint six such council members from leading medical and scientific authorities. The plant would be situated in the capital and would include hospital buildings and facilities, together with buildings which might be devoted to laboratory and experimental work. Under the bill the Federal Works Administration is "authorized to acquire, by purchase, condemnation or otherwise, a site or sites in or near the District of Columbia." Meantime Congress is considering a bill to permit Georgetown University to build a taller medical school hospital than the present law allows. The House District Committee has reported favorably on the request to increase the permitted building height from 90 to 110 feet. Columbia Hospital officials stress urgent need for a nurses' home and training school to be erected after the war.

House Votes to Draft Unmarried Graduate Nurses

By a vote of 347 to 42 the House of Representatives voted to register for the draft virtually all graduate nurses from 20 to 45 years of age, but permitting only unmarried nurses to be subject to induction. All nurses acceptable to the services will be tendered a commission as second lieutenants. All male nurses who are qualified are included, there being about 4,000, of whom 2,000 are in the services but not used as nurses. Widows and divorcées with dependent children are required only to register. Although the measure has yet to have Senate approval, the Army has indicated that it will not back down on its request for a nurse draft. A spokesman for Surg. Gen. Norman T. Kirk, who had just returned from a Pacific tour, said that a draft will produce needed nurses much faster than any voluntary recruitment system.

Miss Mary A. Roberts, editor of the *American Journal of Nursing*, said, in opposition to the measure, "If they draft nurses they will get draft service. You can't draft the spirit of nursing." Officials of the American Nurses Association, with representatives of the Army, Navy, Veterans Administration and Red Cross attending, conferred here to map out plans for a countrywide, direct recruitment campaign, which they said "will give nurses the information they need to straighten out earlier confusion." President Roosevelt, in a telegram to Katharine J. Densford, president of the American Nurses Association, has reasserted his stand on the need of nurse draft legislation as well as intensified efforts to obtain volunteers.

Medical Research to Be Pressed After War

Unsolved problems in medicine will be attacked with the same vigor and success in the coming years of peace as they have under the stimulus of war, Major Gen. James C. Magee, former Surgeon General of the Army, told the forty boy and girl finalists in the fourth annual science talent search conducted by the Science Clubs of America. "The mobilization of scientific talent devoted to medical research in the past few years," he said, "has been productive of enormous benefits to the military establishments and to mankind at large." Examples that he cited were the development of dried plasma and serum albumin as substitutes for whole blood, development of new sulfonamide drugs and the rediscovery and development of penicillin and of DDT. Counseling the youthful scientists to study "pure" science instead of the early tackling of practical problems, Dr. Roger Adams of the Office of Scientific Research and Development said that the men who had the "lucky breaks" in the development of penicillin and the sulfonamide drugs were chemists who were prepared by thorough general training. In connection with the need by industry of scientific knowledge, Maury Maverick, head of the Smaller War Plants Corporation, has urged a "crusade of science" through technical advisory services in every nation to keep industry the world over supplied with information.

Further Assistance for Blind Is Advocated

The armed forces program for blinded men, and efforts to legislate further aid for civilian blind, were lauded by Walter D. Kallenbach, blind evangelist and president of the National Association for the Advancement of the Blind, and Mary Cook Cowerd, blind soprano, who visited Washington to investigate pending legislation for postwar rehabilitation of the sightless. They stressed, however, that what is most vital is an educated public willing to give the blind a chance at normal and interesting careers. Blind persons now working at war jobs will be forced to depend on charity or to turn to selling shoe laces or making brooms, unless employers are openminded about hiring them. Mr. Kallenbach said that the men blinded in war constitute only 1 per cent of the blind population.

Capital Notes

Dr. George C. Ruhland, 65, completing his tenth year as District of Columbia health officer, announced that the Washington death rate had been reduced by 30 per cent since March 1, 1935. Personnel this year totals 2,163, compared with 246 in 1935.

A one week course in automobile driving for amputee patients is being conducted by the American Automobile Association at Walter Reed-Forest Glen Hospital.

The District of Columbia Medical Society has endowed the Davidson Lecture, in honor of Dr. Edward Young Davidson, with the interest from $3,000 to be awarded biennially to a lecturer selected in competition. Essays are to be submitted under a *nom de plume* by physicians or other scientists working in the District.

Official Notes

BUREAU OF INFORMATION SENDS SUMMARY SHEETS TO STATE SOCIETIES

State medical societies have recently been mailed summary sheets by the Bureau of Information for distribution to county societies. The information requested on these blanks relates to the number of physicians in active practice, certain economic conditions of the community and other appropriate details in the counties involved. The early distribution of these sheets to the county societies has been requested. The purpose is to obtain information which will be helpful to areas needing physicians, as well as to physicians seeking locations in which to practice. In order to be of service to communities and to the physicians, it is essential that these summary sheets be returned promptly. As soon as the data are supplied they can be used to aid medical officers separated from service. Lieut. Col. Robert D. Bickel, M. C., liaison officer to the American Medical Association from the Surgeon General's Office, is tabulating the information as soon as received, so that it can be made available at once to discharged medical officers. State and county society executives to whom these summary sheets are sent are urgently requested to expedite the completion and return of this material.

AMERICAN MEDICAL ASSOCIATION-N. B. C. NETWORK PROGRAM

Doctors Look Ahead on March 17 is to be devoted to an appeal to the women of the United States to meet the need for Army and Navy nurses and for medical technicians. Graduate nurses eligible for commission are urgently needed, and so are women members of the WAC who can be trained to perform simple technical procedures in the laboratories and thus release more highly trained personnel for the complicated procedures. Public service of this type has been performed frequently as a part of Doctors Look Ahead and previous American Medical Association and National Broadcasting Company programs.

Inquiries have been received by the Bureau of Health Education asking for transcriptions of Doctors Look Ahead. These network programs should not be confused with the transcribed programs also available. When a program has been broadcast on a nationwide network transcriptions are useless because no radio station will use an identical program a second time except in rare instances where programs of unusual merit are rebroadcast by request.

Doctors Look Ahead is heard on one hundred and twenty-three stations of the National Broadcasting Company network each Saturday at 4 p. m. Eastern War Time (3 p. m. Central War Time, 2 p. m. Mountain War Time and 1 p. m. Pacific War Time). Some stations may record the program and broadcast it at a time which suits their schedule better. Local newspaper radio announcements should be consulted.

The next four programs deal with the following topics:

March 17.—Women at War, in cooperation with the Office of War Information. The speaker will be Major Gen. Norman T. Kirk, Surgeon General, U. S. Army.
March 24.—Juvenile Delinquency.
March 31.—Accidents.
April 7.—Tuberculosis.

Council on Medical Service and Public Relations

PUBLIC RELATIONS MEETING IN VIRGINIA

A detailed discussion of public relations in all its phases was held by the Arlington County Society of Virginia on February 19. This meeting was attended by Dr. Joseph S. Lawrence, who described the Washington Office of the Council and answered questions concerning its work. Many physicians who attended expressed the desire that the Council develop an active public relations program "that would extend beyond the medical profession." The Arlington group also expressed a desire for definite information as to the development of voluntary insurance plans by state and county medical organizations.

The meetings which Dr. Lawrence has attended include the Legislative Conference of the Indiana State Medical Association, Secretaries' Conference of the Michigan State Medical Society, Conference of County Medical Society Secretaries and Editors of the Medical Society of the State of Pennsylvania, at which he spoke on "Realism in Public Relations," Toledo Academy of Medicine, the Cabell County Medical Society of West Virginia and the Arlington County Medical Society.

REGIONAL CONFERENCES DURING APRIL

The Council on Medical Service and Public Relations has scheduled three regional conferences on the West Coast during April. These conferences, which are to be held in Portland, Ore., San Francisco and Los Angeles, will complete a series of seven formal regional meetings and one informal session held by the Council. Representatives from eleven states and Alaska have been invited to attend the April meetings, each of which will include a morning program by speakers from various bureaus and departments of the American Medical Association and an afternoon question and answer round table discussion.

The schedule for these meetings follows:

April 7. Northwest Conference, Portland, Ore., for Oregon, Washington, Idaho, Montana, Wyoming and Alaska.
April 10. Northern California Conference, San Francisco, for Nevada, Colorado, Utah and northern California.
April 13. Southern California Conference, Los Angeles, for southern California, New Mexico and Arizona.

In addition to the regional meetings the representatives of the American Medical Association will attend the House of Delegates meeting of the Oregon State Medical Association to be held April 8 in Portland. Representatives of the American Medical Association who will appear on the program will be Dr. John H. Fitzgibbon, Portland, Ore., Chairman of the Council; Dr. E. J. McCormick, Toledo, Ohio, Vice Chairman of the Council; Dr. Joseph S. Lawrence, Washington, D. C., Director of the Washington Office of the Council; Mr. J. W. Holloway Jr., Director of the Bureau of Legal Medicine and Legislation; Dr. Carl Peterson, Secretary of the Council on Industrial Health; Mr. Thomas A. Hendricks, Secretary of the Council on Medical Service and Public Relations, and Dr. Victor Johnson, Secretary of the Council on Medical Education and Hospitals, who is on the program for the San Francisco and Los Angeles meetings.

Woman's Auxiliary

Indiana

The Woman's Auxiliary to the Indiana State Medical Association has urged all of its members to carry a copy of *Hygeia* to all Parents and Teachers Association and club meetings as a means of promoting its distribution. "Hygeia for Health" has been their suggested slogan.

New York

Dr. Nathan B. Van Etten and Mr. Dwight Anderson addressed the executive board meeting of the Woman's Auxiliary to the Medical Society of the State of New York January 24 and 25. The subject was "The Woman's Auxiliary and Medical Public Relations."

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Changes in Health Officers.—Dr. Albert F. Zipf, health officer of Sacramento County, has taken over the activities of the health officer of Sacramento, Dr. Herbert F. True, who retired because of ill health.——Dr. Wayne P. McKee has been named health officer of Ferndale in Humboldt County, succeeding Dr. Herbert C. James.

Seminar on Advanced Psychotherapy.—Dr. Frieda Fromm-Reichmann, director of psychotherapy at Chestnut Lodge Sanitarium, Rockville, Md., will give a seminar on advanced psychotherapy in San Francisco, March 26-April 2, under the auspices of the department of psychiatry of the University of California Medical School, Stanford University School of Medicine and the Mount Zion Hospital.

Research on Epilepsy.—A gift of $2,000 from Mr. and Mrs. Eugene Fowler, Newcastle, has been made to the University of California Medical School, San Francisco, to be known as the Mother Lode Fund, with the request that it be used in research on epilepsy. The work will be carried out at the University of California Hospital under the direction of Dr. William J. Kerr, professor of medicine in the medical school.

Health Board to Observe Seventy-Fifth Anniversary.—On April 15 the seventy-fifth anniversary of the organization of the California State Department of Public Health will be observed. The department is said to be the second of the kind to be established in the United States, the first being the Massachusetts Department of Public Health (THE JOURNAL, January 20, p. 173). According to *California's Health*, the official bulletin of the state health department, the transcontinental railroad was completed only a few months before the creation of the board, and the enactment of progressive legislation to establish the California state board of health at this early period is a noteworthy event.

DISTRICT OF COLUMBIA

History of District Society Completed.—After two years of research Dr. John B. Nichols, Washington, chairman of the committee on history, has completed writing the history of the Medical Society of the District of Columbia from the time of its organization to the present day. Serving with Dr. Nichols on the committee on history have been Drs. William J. Mallory and Joseph S. Wall.

GEORGIA

Twenty-Five Years of "Georgia's Health."—The January issue of *Georgia's Health*, the official bulletin of the Georgia Department of Public Health, marked the completion of twenty-five years as a health education medium.

Hospital News.—The Emily Winship Woodruff Maternity Center of Crawford W. Long Memorial Hospital, Atlanta, has been opened. The nine story building was begun in 1941, but work was delayed because of lack of essential materials. The new unit has all the accommodations needed for the expectant mother, and patients coming to the center who are not able to pay regular fees may have services for $27.50.

Ophthalmic Seminar at Emory University Canceled.—Emory University School of Medicine, Atlanta, announces the cancellation of the ophthalmic seminar scheduled to be held in Atlanta April 19-21, planned to honor the memory of Dr. Abner Wellborn Calhoun, the first professor of ophthalmology at Atlanta Medical College, which was established in 1854 and which in 1915 became the school of medicine of Emory University. Dr. Calhoun was born April 16, 1845 and died Aug. 21, 1910.

IDAHO

Physician Senator Resigns.—Dr. Charles A. Robins, St. Maries, has resigned as state senator because he is the only physician and surgeon in Benewah County, according to *Northwest Medicine*.

State Medical Board.—Drs. Hoyt B. Woolley, Idaho Falls, Robert L. Rodwell, Nampa, and Glenn McCaffery, Kellogg, were recently appointed members of the state board of medical examiners. Reappointments include Drs. George C. Halley, Twin Falls, Samuel M. Poindexter, Boise, and Clifford O. Armstrong, Moscow.

ILLINOIS

Chicago

New Health Editor of Chicago Tribune.—Dr. Theodore R. Van Dellen, medical consultant to the Chicago *Tribune* since 1941, has been appointed health editor, succeeding the late Dr. Irving S. Cutter. Dr. Van Dellen graduated at Northwestern University Medical School in 1936.

Branch Society Meeting.—The North Side Branch of the Chicago Medical Society will meet at the Drake Hotel, April 5. Speakers will be Dr. Edwin C. Hamblen, Durham, N. C., on "Functional Uterine Bleeding"; Frank X. Gassner, D.V.M., Fort Collins, Colo., "Some Endocrine Problems in Veterinary Medicine," and Warren O. Nelson, Ph.D., Iowa City, "Endocrine Factors in the Development and Function of the Breast."

Readjusting with the Returning Servicemen.—The readjustment from war to peace must take into consideration the emotional as well as the physical and material needs of soldier and civilian; the conditioning of the civilian for the soldier's return and the renaturalization of the soldier was the theme of the thirty-sixth annual meeting and two day institute sponsored by the Illinois Society for Mental Hygiene, March 8-9 at the Knickerbocker Hotel. Among the speakers were:

Dr. Rudolph G. Novick, Elgin, Ill., medical director, Illinois Society for Mental Hygiene, The Conference Theme.
Col. William J. Bleckwenn (MC), He Takes Off His Uniform.
Lieut. Comdr. Louis A. Schwartz (MC), Emotional Disorders in the Disabled Veteran.
Francis Rosecrance, Ph.D., Evanston, Emotional Aspects of Educational Problems.
Harold Taylor, employment manager, Hawthorne Works, Western Electric, Emotional Aspects of Industrial and Employment Problems.
Dr. Gregory Zilboorg, New York, Psychosocial Paradoxes of Returning from the War.
Marguerite G. Nordman, director of home service, St. Louis chapter, American Red Cross, Helping in the Readjustment of the Soldier and His Family.
Dr. George S. Stevenson, New York, Rebirth of a Civilian.

Three round table discussions covering industry, education and religion formed a part of the second day's session.

INDIANA

Constitution Amended to Permit Physician on Board.—For the first time since the General Hospital Association of Elkhart was organized in 1909, a doctor of medicine has been elected to its board of directors. It was necessary to change the constitution to provide for the addition of Dr. David D. Todd, head of the surgical section of the medical staff at the Elkhart General Hospital, who was chosen to succeed Mrs. Cora Elliott, secretary of the board. To place Dr. Todd on the board the constitution was amended to read "any citizen over the age of 21 years, residing in the city of Elkhart, shall be eligible to serve as a director of the association." The exception removed from the constitution read "excepting physicians, surgeons, dentists, osteopaths, the practitioners of any healing cult or science, and clergymen." Newspapers reported that Dr. Todd made the motions for the amendments, stating that a physician on the board could help with the administration of the hospital, get cooperation of the nursing staff as well as the nonprofessional staff of the hospital, maintain the good will of the hospital and assist in solving the medical problems of the future.

Governor Outlines Health Program.—On January 25 Governor Gates outlined legislative program of his administration for general expansion of the state's health service facilities, according to the Indianapolis *Times*. Among his recommendations was the reorganization of the state board of health, increasing its membership from four to seven to include three physicians, one dentist, one sanitary engineer, one pharmacist and one woman who has "demonstrated interest in public health." The bill carrying this recommendation, now passed and signed by the governor, includes a nurse and a veterinarian as members of the board, bringing the total to nine. Other recommendations include:

Creation of full time health boards or departments in all towns and smaller cities.
Creation of a state board to recodify all state health laws for enactment by the 1947 legislature.
Legislation authorizing cities and counties to create funds for the construction of health centers and clinics through endowments, subscriptions or direct appropriations.
Creation of two new divisions under the state health board, one for dealing with diseases of aged persons and a dental health department.
Strengthening of laws on tuberculosis quarantine, compelling persons unwilling to be committed to be examined by a three physician board.
An inspection service and licensing by state health board of hospitals practicing medicine, surgery and obstetrics, extending control over present maternal and child health service.
Expansion of the stream pollution control board from six to seven members.

IOWA

State Meeting Canceled.—The Iowa State Medical Society has canceled its annual session, scheduled to be held in Des Moines April 19-20.

KANSAS

Infectious Jaundice in Riley County.—Twenty-seven cases of infectious jaundice were recently reported in Riley County, 16 from Manhattan and 11 from Ogden. The local health department, of which Dr. Fred P. Bestgen, Manhattan, is director, and the laboratory at the Kansas State College of Agriculture and Applied Science, Manhattan, assisted with diagnostic procedures, with consultation service from Dr. Clarence H. Kinnaman, Topeka, state epidemiologist, and C. A. Hunter, Ph.D., Topeka, director of laboratories, state board of health, according to the *News Letter*. Of the Riley County cases 14 were in children between the ages of 5 and 15 years and there were 4 cases in children less than 5 years of age, 4 cases in persons 25-29 years of age, 2 in the 50-54 year age group and 1 case each in the 15-19, 45-49 and 70-74 year age groups. Although most families in which cases occurred owned dogs as family pets and the highest incidence was in children from 5 to 14 years of age who would be likely to play with dogs, health authorities emphasized the present need for rat control and stressed careful washing of all foodstuffs to remove possible contamination from both rats and dogs.

LOUISIANA

State Meeting Postponed.—The annual meeting of the Louisiana State Medical Society, scheduled to be held in New Orleans April 13, has been postponed.

Hospital News.—The new War Memorial Hospital, Leesville, was recently opened at a cost of $250,000. The unit is one story high with buff brick exterior.

University News.—Beginning with the session of 1944-1945, Tulane University of Louisiana School of Medicine, New Orleans, broke the tradition of starting the freshmen students with the dissection of the human body by substituting instruction in biochemistry instead of gross anatomy, which has heretofore been delayed until the study of physiology is started in the latter part of the first year. The *Bulletin* of the Tulane Medical Faculty states that it is believed that the change will make for an easier transition from the premedical studies to those of the medical curriculum.

MASSACHUSETTS

Hospital News.—Plans have been announced to construct a new building for the New England Deaconess Hospital, Boston, to be eight stories high and accommodate 200 patients. A campaign has been started by the hospital to raise $1,500,000 to finance the project.

Frederick Bailey Named Health Commissioner of Boston.—Dr. Frederick J. Bailey, Boston, who has been associated with the Boston Health Department almost continuously for the past forty years, was recently appointed health commissioner of Boston to succeed Dr. George Lynde Gately, now in the Navy. Dr. Bailey, who graduated at Harvard Medical School, Boston, in 1903, has been serving recently in the U. S. Naval Reserve.

Personal.—William L. Campbell, formerly of Berlin, N. H., has been appointed head of a new department devoted to education and research in food technology at the Massachusetts Institute of Technology, Cambridge. The new department will expand and extend the scope of the Samuel Cate Prescott Laboratories of food technology, of which Bernard E. Proctor, Ph.D., was recently appointed director (THE JOURNAL, February 10, p. 346).

MICHIGAN

Personal.—Dr. Emil Amberg, Detroit, was recently elected to emeritus membership in the Michigan State Medical Society. ——Dr. William M. LeFevre has been appointed a member of the Muskegon board of health to succeed the late Dr. Samuel A. Jackson.

Raymond Hussey Honored.—Dr. Raymond Hussey, newly appointed dean of the School of Occupational Health and professor of preventive medicine at Wayne University Medical Science Center, Detroit (THE JOURNAL, February 17, p. 411), was guest of honor at a dinner February 28 sponsored by the committee on medical education of the Wayne County Medical Society. Dr. Hussey spoke on "The Future Development of Industrial Health Education in the United States."

Health Officers Association Created.—Dr. Clarence D. Barrett, Mason, was elected president of the recently organized Michigan Health Officers Association, which was set up to advance public health principles and practices, to recommend standards of employment based on education, training and experience, to make community health protection more complete and certain through study and conference with proper authorities and to strive for a good program for the retirement of health officers and staff members with pension and to seek legislative enactment to this end. Other officers include Drs. Otto K. Engelke, Ann Arbor, vice president, and Vladimir K. Volk, Saginaw, secretary-treasurer.

Industrial Medical and Surgical Conference.—The third annual postgraduate industrial medical and surgical conference, sponsored by the committee on industrial health of the Michigan State Medical Society in cooperation with the department of postgraduate medical education of the University of Michigan, will be held in Detroit, April 5. Among the speakers will be:

Drs. Winfred B. Harm and Earle A. Irvin, Detroit, Industrial Medicine—Cooperation Between Industrial Physicians and Private Practitioners.
Theodore P. Ryan, LL.B., Lansing, Problems Arising from Michigan's New Compensation Law.
Dr. Dudley A. Irwin, Pittsburgh, Treatment and Prevention of Silicosis with Aluminum Powder.

At a symposium on postwar problems of industrial health and medicine, at which Dr. Raymond Hussey, Detroit, will be the leader, participants include:

O. L. Beardsley, Detroit, Selective Placement of Workers—A Personnel Manager's Viewpoint.
Dr. Fenn E. Poole, Burbank, Calif., Selective Placement of Workers—A Medical Man's Viewpoint.
Dr. H. Graham Ross, Montreal, Psychosomatic Medicine in Industry.
Major Roy P. Warren, S. C., Health Maintenance Engineering in Relation to Industrial Health.

Presiding at the sessions will be Drs. Andrew S. Brunk, Detroit, president of the state medical society, Kenneth E. Markuson, Lansing, chairman of the state industrial health committee, general chairman, and Patrick L. Ledwidge, Detroit.

NEW JERSEY

Personal.—Dr. Leslie Robert Angus, senior psychiatrist with the Institute of Living, Hartford, Conn., has been appointed medical director of the Bancroft School, Haddonfield.

Colonel Ash to Give Martland Lecture.—Col. James E. Ash, director, Army Institute of Pathology, Office of the Surgeon General, Washington, D. C., will deliver the tenth Harrison S. Martland Lecture at the Academy of Medicine, Newark, March 28, under the auspices of the Essex County Anatomical and Pathological Society. Colonel Ash's subject will be "The Army Institute of Pathology and Its Contribution to the Study of Diseases Prevalent in the Military Air Group."

NEW YORK

Meeting Canceled.—The Medical Society of the State of New York has canceled its annual meeting, scheduled to be held in Buffalo April 30-May 3.

Seminars on Rheumatic Fever.—The St. Francis Sanatorium for Cardiac Children, Roslyn, opened a course of seminars on rheumatic fever and rheumatic heart disease March 8 to continue once a week on Thursday. Demonstration of clinical material will be stressed at these conferences. Dr. Leo M. Taran is medical director of the sanatorium.

Resignations in State Health Department.—Dr. Augustus B. Wadsworth, director of the division of laboratories and research, New York State Department of Health, Albany, retired January 31 after thirty-one years of continuous service. Dr. Marion F. Loew, assistant director of the division of maternity, infancy and child hygiene since 1936, retired from state service February 23. *Health News* reports that she will go to Antioch College, Yellow Springs, Ohio, to join the Samuel S. Fels Research Institute.

Graduate Lectures.—The Cortland County Medical Society will be addressed April 20 by Dr. Edward C. Hughes, Syracuse, on "Hemorrhages of the Latter Part of Pregnancy" and Dr. Orren D. Chapman, Syracuse, May 18, on "Diagnosis and Treatment of Meningitis." The Jefferson County Medical Society will be addressed April 12 by Dr. Clarence E. da la Chapelle, New York, on "Management of Acute Cardiovascular Emergencies." These lectures are sponsored through the cooperation of the state medical society and the state department of health.

New York City

Caroline Zachry Dies.—Caroline B. Zachry, Ph.D., director since May 1942 of the bureau of child guidance of the city school system, died February 22, aged 50.

Appointments to Metropolitan Life.—The board of directors of the Metropolitan Life Insurance Company has made the following appointments, effective February 20:

Dr. Albert O. Jimenis to associate medical director.
Dr. Haynes H. Fellows to associate medical director.
Dr. Anthony J. Lanza to associate medical director.
Dr. George M. Wheatley to be assistant vice president, welfare.

Bequest to Finance Work in Psychiatry.—The Lester N. Hofheimer estate has granted $35,000 to Columbia University College of Physicians and Surgeons to finance the first year's expenses of the newly created Psychoanalytic and Psychosomatic Clinic for Training and Research (THE JOURNAL, Sept. 23, 1944, p. 247). The grant comes from the estate of Lester N. Hofheimer, first lieutenant, Army Air Forces, who was killed in India in December 1943 and is the first made in the field of psychiatry under the lieutenant's will, according to *New York Medicine*. Lieutenant Hofheimer left the bulk of his estate, approximating one million dollars, to philanthropic enterprises, the distribution of which is left to the discretion of three executors (THE JOURNAL, June 24, 1944, p. 588).

Deaths from Carbon Monoxide.—Escaping gas containing carbon monoxide killed 325 persons in New York City during 1944, 289 of the deaths occurring in homes. In a release to the press Dr. Ernest L. Stebbins stated that these are preliminary figures and that when the final returns were completed the total would probably be somewhat higher. The National Safety Council on January 15 reported that gas asphyxiation fatalities have increased 50 per cent since the beginning of the war. Gas killed 1,800 Americans in their homes during 1943, council statistics show. Carbon monoxide, dangerous because it is both colorless and odorless, caused most of these deaths. One fifth of these fatalities were caused by coal gas, mostly carbon monoxide, produced when stoves, furnaces or flues are defective or when dampers are not properly set. About half of the deaths were caused by illuminating gas. Makeshift arrangements to supplement rationed heat and badly worn equipment were named by the council as contributors to the increase. Poorly adjusted burners and leaky fittings are chief offenders.

NORTH CAROLINA

Personal.—Dr. James S. Gamble has been named superintendent of the Reeves Gamble Hospital, Lincolnton, and local surgeon for the Seaboard and Southern Railways succeeding his father, the late Dr. John R. Gamble.——Dr. Sigma V. Lewis has been appointed director of the Burke-Caldwell district health department with offices in Lenoir.

Pellagra Declines.—Fewer persons died of pellagra in North Carolina in 1944 than during any other year for which the records are available. For the entire year only 64 such deaths were reported to the state board of health and an all time low rate of 1.7 was recorded. During the previous year there were 110 deaths from this malnutrition disease, and the rate was 3.0. These figures are in sharp contrast with those of former years. In 1918, the peak year of United States participation in the first world war, the pellagra death rate in North Carolina was 25.7, and in 1929 and 1930, which were depression years, the rates rose to 32.0 for each year, after a recession that followed the war and coincided with "prosperity." With the easing of the depression the pellagra death rate again began to decline, but not to any considerable degree until after 1937. The rate that year was 13.0, but in 1938 it dropped to 7.3, and the down trend has been sustained since that time, being 5.9 in 1939, 4.7 in 1940, 3.8 in 1941, 3.0 in 1942 and 1943 and 1.7 in 1944, the lowest ever recorded. The general death rate in the state was 7.9 as compared with 8.1 the previous year. The infant mortality rate dropped to 44.7, a new all time record, and the maternal death rate fell to 2.9, also a new low rate for the state. A birth rate of 24.7 was recorded.

OKLAHOMA

State Meeting Canceled.—The Oklahoma State Medical Association has canceled its annual meeting, scheduled to be held in Oklahoma City.

Society Resumes Publication of Bulletin.—The Garfield County Medical Society recently voted to resume publication of its monthly journal, the *Bulletin*. Publication of the bulletin was suspended when Dr. Roscoe C. Baker, Enid, entered the armed forces but, according to the *Journal of the Oklahoma State Medical Association*, he will have charge of the work when it is again printed.

County Society Enlarges Quarters.—The executive offices of the Tulsa County Medical Society, 1202 Medical Arts Building, Tulsa, have been remodeled following an addition of a large room to the society quarters. The medical library has been expanded, and separate offices have been constructed for the executive secretary. The medical credit bureau has also been enlarged. The Tulsa County Medical Society now utilizes the entire twelfth floor of the Medical Arts Building.

PENNSYLVANIA

Philadelphia

Dr. Blechschmidt Honored.—Dr. Dorothy C. Blechschmidt was honored at a luncheon recently given by the One Hundred Club of Philadelphia in recognition of her work at the Blechschmidt Cancer Prevention Clinic, located in the Doctors Hospital. The clinic was organized about three years ago and is named for Dr. Blechschmidt, who serves as its chief of staff. It is financed by a membership of almost 1,000 women; no salaries are paid, for all the service is voluntary (THE JOURNAL, July 1, 1944, p. 665). The One Hundred Club is an organization composed of past and present presidents of various organizations in Philadelphia.

Annual Health Institute.—The woman's auxiliary to the Philadelphia County Medical Society will hold its fifteenth annual health institute April 10 in the auditorium of the Philadelphia County Medical Society. "Health Problems in Wartime" will be the theme of the meeting. Among the speakers will be:

Col. Leonard G. Rowntree, M. C., Physical Fitness.
Dr. Rufus S. Reeves, Poliomyelitis.
Dr. Samuel B. Hadden, War Neuroses.
Mrs. David W. Thomas, president of the Woman's Auxiliary to the American Medical Association.
Hon. Nochem S. Winnet, judge of Municipal Court, The Judge Looks at Juvenile Delinquency.
Dr. John H. Stokes, Problem of Human Relations as It Relates to Social Hygiene.
Lieut. Col. James B. Brown, M. C., Reconstructive Surgery.

The session will also be addressed by Dr. Charles L. Brown, president of the Philadelphia County Medical Society, and Dr. William Bates, president of the Medical Society of the State of Pennsylvania. Mrs. S. Dale Spotts, president of the woman's auxiliary of the county society, will preside at the meeting.

Colonel Ravdin Named to Barton Professorship.—Col. Isidor S. Ravdin, M. C., who is in command of an army hospital in India while on leave of absence from the University of Pennsylvania School of Medicine, has been appointed John Rhea Barton professor of surgery. Colonel Ravdin graduated at the University of Pennsylvania School of Medicine in 1918 and has been Harrison professor of surgery and director of the Harrison department of surgical research in the school of medicine since 1936; prior to that time he held other faculty posts, including the J. William White professorship of surgical research. Dr. Eldridge L. Eliason, who is now the Barton professor and a member of the faculty since 1907, planned to retire on July 1 but will continue for the present while Colonel Ravdin is on active service. Dr. Eliason graduated at the University of Pennsylvania School of Medicine in 1905 and joined the teaching staff as assistant instructor in surgery. In 1925 he was appointed professor of clinical surgery in the school of medicine and the following year to a similar post in the graduate school of medicine of the university. He has been John Rhea Barton professor of surgery since 1936 and professor of surgery in the graduate school of medicine since 1938.

UTAH

Three Man Committee Acts as Dean.—A committee of three members of the faculty of the University of Utah School of Medicine, Salt Lake City, has been appointed to direct the activities of the school, pending the appointment of a dean to succeed Dr. A. Cyril Callister, resigned (THE JOURNAL, February 10, p. 347). Members of the committee include Dr. Charles E. McLennan, professor and head of the department of obstetrics and gynecology, chairman, and Dr. Hyrum L. Marshall, professor and head of the department of public health and preventive medicine, and Chester A. Swinyard, Ph.D., associate professor of anatomy. The committee will serve in all administrative affairs of the school of medicine until the appointment of a new dean. Dr. Callister plans to return to the private practice of medicine, it was reported.

WASHINGTON

Reject Proposed Ban on Foreign Physicians.—A proposed ban by the King County Medical Society on membership of physicians educated outside the United States and Canada was rejected unanimously at a meeting of the society January 8. It was stated that the proposal was submitted with the idea that it is difficult in these times to check on the credentials of men educated in European medical schools. It was decided, however, that such action would be untimely.

Research Foundation Set Up in County Hospital System.—The establishment of the Foundation for Medical Research of the King County Hospital System was announced at a recent meeting of the medical board of the system in Seattle. According to the *Bulletin* of the King County Medical Society it is anticipated that the fund, of which $25,000 is now available, will be of considerable interest to the community, as it will be open for donations and bequests to any one interested in promoting the advancement of knowledge in medicine, surgery and all of their branches. Administration of the fund will be placed directly in the hands of a committee of local physicians working under the direction of the board of trustees of the county hospital, and it is anticipated that it will grow to have considerable significance in cooperating in the development of research at the new medical-dental school of the University of Washington.

WEST VIRGINIA

Proposed Merger of Health Departments.—Merger of the health departments of the city of Charleston and Kanawha County has been recommended by Dr. Elias W. Langs, U. S. Public Health Service Reserve, who conducted a survey and made an exhaustive study of the matter early in the winter in cooperation with Dr. John E. Offner, Weston, state health commissioner. The survey, which followed the recommendation of the state medical association's fact finding and planning committee that all city health departments be merged with the health department of the county in which the unit is located, was made with the full consent of city and county officials. In his report Dr. Langs recommended that within two years after the merger all affiliated health agencies, including the entire school health service, be consolidated with the unit, which would be under the direction of an experienced health officer. Administration would be under the supervision of a nonpartisan board of health.

WISCONSIN

Position Available as Director of Laboratories and Research.—The Milwaukee City Service Commission announces an examination to fill the position of director of laboratories and research in the city health department. Additional information may be obtained from the Milwaukee City Service Commission, Room 716, City Hall, Milwaukee 2.

Lewis Danziger Wins Rogers Essay Contest.—Dr. Lewis Danziger, on the staff of the Milwaukee County Hospital for Mental Diseases, has been announced as the winner of the Rogers Memorial Essay Contest, sponsored by the Milwaukee Academy of Medicine and founded by the Rogers Memorial Sanitarium. Dr. Danziger won the first prize of $200 for his manuscript on "Anoxia and Compounds Causing Mental Disorders in Man." The contest was established in 1943 (THE JOURNAL, June 19, 1943, p. 553).

Personal.—Dr. Mark A. Bailey was recently appointed health officer of Fennimore.——Dr. Valentine A. Gudex, Milwaukee, has resigned as deputy state health officer; he was connected with the state board of health for twenty-six years. ——Edwin Broun Fred, Ph.D., professor of bacteriology at the University of Wisconsin, Madison, since 1943 dean of the college of agriculture, previously for nine years dean of the graduate school, has been elected president of the university to succeed Clarence A. Dykstra, LL.D., who has become provost of the University of California at Los Angeles.

Diagnostic Center Proposed.—The tentative plans to develop a diagnostic center in Wisconsin have been approved by an advisory committee of the state medical society to the state department of public welfare and its committee on public policy. The University of Wisconsin, Madison, has also pledged its cooperation. As outlined in the state medical journal, the building would be constructed in Madison close to the State of Wisconsin General Hospital to accommodate 150 persons who have been committed to one of the certain state correctional institutions and for occupancy by persons placed on probation to the department of public welfare. The administration of the center is to be the function of the department of public welfare. The center would provide for the complete medical examination of all those, except those going to either Mendota or Winnebago, who are committed to the care of the department of public welfare and whom the state will either attempt to adjust to a more conventional behavior or resort to a useful functioning capacity. It is expected that the building would cost about $700,000 and that about $116,000 would be needed to maintain it annually. The new project would care for the large group of young people who come under the care of the department of public welfare for whom no adequate medical facility now exists and who cannot be accommodated by the two state hospitals concerned with mental diseases. It is believed that the proposed diagnostic medical center and its location near the medical school of the state university would assist the state department of public welfare in developing a program of rehabilitation in this class of young people for whom accommodations are not otherwise available.

HAWAII

Industrial Group Changes Name.—The Territorial Association of Plantation Physicians is the name by which the component society of the American Association of Industrial Physicians and Surgeons, heretofore known as the Hawaiian Society of Industrial Physicians and Surgeons, will be known.

Graduate Course.—A postgraduate course was conducted for the Honolulu County Medical Society, January 8-14, in the Mabel Smyth Auditorium, Honolulu. Members of the armed forces stationed in Honolulu presented the program, which included round table discussion on the specialties and a symposium on cardiovascular disease, neuropsychiatry, cancer and diseases of the chest.

Hawaii's Medical Service Plan.—A program of medical and hospital service has been functioning in Honolulu under the auspices of the Honolulu County Medical Society and now has a participating membership of nearly 10,000 and is pointed in a direction of complete coverage. Members of the Territorial Medical Association of Hawaii are considering expansion of the plan, currently restricted to the island of Oahu, throughout the territory. Mr. Reginald W. Carter, general manager of the Hawaii Medical Service Association which operates the Honolulu Medical and Hospital Plan, is traveling throughout the United States visiting various installations which deal with medical and hospital care. His tour included several days at the headquarters of the American Medical Association studying the program of the Council on Medical Service and Public Relations. Information concerning the Hawaii plan, which was established in 1938, may be obtained by addressing Mr. Carter at Room 417, Hawaiian Trust Building, Honolulu.

GENERAL

Society News.—At a special meeting of the board of trustees of the United States Pharmacopeial Convention Robert L. Swain, Sc.D., New York, was elected chairman to fill the vacancy caused by the recent death of former chairman Evander F. Kelly, Sc.D. Dr. Swain was elected a member of the board in 1936 and was reelected by the convention at its 1940 meeting in Washington, D. C.

Meetings Postponed.—At a meeting of the council of the American Psychiatric Association in Chicago, February 26-27, it was voted to postpone the annual session of the association, scheduled to be held in Chicago May 21-24, until August 26. Dr. Winfred Overholser, St. Elizabeths Hospital, Washington 20, D. C., is secretary-treasurer of the American Psychiatric Association.——The executive board of the American Public Health Association has voted to postpone the seventy-fourth annual meeting of the association, scheduled to be held in Chicago the week of September 17.

National Noise Abatement Week.—April 29 to May 5 has been designated National Noise Abatement Week. Again the National Noise Abatement Council will make its annual awards for civic achievements in the abatement of needless noise, consisting of one grand national award and four city population class awards. A gold plaque symbolic of the award will be presented to the grand national award winner, and a silver plaque will be given to the winning city in each population group. These plaques, designed by the eminent sculptor Rene Paul Chambellan, depict Aeneas, hero of Vergil's Aeneid, overcoming the many headed monster Cerberus, who guarded

the gates to Hades. In vivid bas-relief Aeneas is portrayed in the act of hurling bits of drugged food into the jaws of the beast, which, according to Vergil's tale, effectually quells Cerberus, who falls asleep.

Information Bulletin on Rehabilitation and Reconditioning.—The Baruch Committee on Physical Medicine is making available without charge a bulletin of information on "War and Postwar Rehabilitation and Reconditioning." The booklet, which may be obtained on request through the committee, 597 Madison Avenue, New York 22, contains up-to-date reports on the recent activities in reconditioning and physical rehabilitation from the Army Reconditioning Division, from the Rehabilitation Division of the Medical Department of the Navy, from the Convalescent Training Division of the Army Air Forces, from the Division of Physical Medicine and Medical Rehabilitation of the Veterans Administration, from the Committee on Convalescence and Rehabilitation of the National Research Council and from the Federal Security Agency concerning the Federal-State Program of Vocational Rehabilitation for the Civilian Disabled. A report concerning the activities of the Baruch Committee appeared in THE JOURNAL, Dec. 9, 1944, page 973.

Meetings Canceled.—The National Tuberculosis Association has canceled its annual meeting, which was to be held in Buffalo June 13-15. The *Bulletin* of the National Tuberculosis Association states that the board of directors of the association, the executive committee of the National Conference of Tuberculosis Secretaries and the council of the American Trudeau Society will hold meetings on dates to be announced later.——The Federation of American Societies for Experimental Biology has canceled its annual session, which was to be held in Cleveland May 8-10. The federation is composed of the American Physiological Society, American Society of Biological Chemists, American Society for Pharmacology and Experimental Therapeutics, American Society for Experimental Pathology, American Institute of Nutrition and the American Association of Immunologists.——The American Society for Clinical Investigation has canceled its annual meeting, which was to have been held in Atlantic City May 7. Dr. Wesley W. Spink, University Hospitals, Minneapolis 14, is the secretary.

Snow Medal Awarded to Merritte W. Ireland.—The presentation of the William Freeman Snow Medal for distinguished service to humanity to Major Gen. Merritte W. Ireland, formerly surgeon general of the U. S. Army, was a feature of the thirty-second annual meeting of the American Social Hygiene Association in Chicago recently. Honorary life memberships in the association were presented to Drs. Bertha M. Shafer, Chicago, director, Illinois Social Hygiene League, and Lieut. Col. Donald H. Williams, chief, division of venereal disease control, National Department of Health and Welfare, Canada. Thomas Parran, surgeon general of the U. S. Public Health Service, addressed a session on "Social Hygiene, the Past Five Years and the Next Five Years." The thirty-second annual session of the American Social Hygiene Association was held in conjunction with the Chicago Conference on Social Hygiene and speakers included:

Dr. C. Walter Clarke, New York, executive director, American Social Hygiene Association, Present and Future Public Health Problems in Social Hygiene.

Henry L. McCarthy, Chicago, director, Region No. VI, Social Security Board, Social Protection Program in Action.

Mrs. Bertha Ashby Hess, chief, bureau of health education, Cleveland Health Department, Responsibility of the High Schools in a Social Hygiene Education Program.

Dr. Herman N. Bundesen, president, Chicago Board of Health, Chicago Rapid Treatment Program.

One session was devoted to "Industry versus Venereal Disease."

FOREIGN

Psychiatrist Shot as Hostage.—Dr. Haakon Saethre, director of the psychiatric department of the General Hospital in Oslo, was arrested when at work in the hospital a short time after the police general of the Quisling party of Norway, called the Norwegian Heydrich, was machine gunned to death on the street in Oslo by the Norwegian home forces, February 8. Dr. Saethre was among the prominent members of liberal professions who were arrested and shot or sentenced by the German Standgericht. According to a communication, Dr. Saethre was selected as a victim because he was known for his unhesitating patriotism. The tragedy of Dr. Saethre's death recalls another incident nearly four years ago, the communication stated, when another prominent Norwegian psychiatrist, Dr. Rolf Gjessing, was arrested because he would not accept an inferior Quisling as superintendent of male nurses at his hospital. When Norwegian physicians as a body threatened to strike, the Quislings released Dr. Gjessing.

Deaths in Other Countries

Lord Dawson of Penn, physician to four kings and first Viscount, died March 7 of pneumonia, aged 80. Lord Dawson became physician in ordinary to Edward VII in 1907. He continued in the same post with George V, Edward VII and the present George VI. Although still convalescing from an operation performed a number of months ago he was recently consulted about the health of David Lloyd George, prime minister of Britain in the first world war. He was formerly president of the British Medical Association.

Government Services

Proceedings of Conference on Rheumatic Fever

Proceedings of the national conference on state rheumatic fever programs, held at the Children's Bureau in the fall of 1943, have just been published, and copies are available free on request to the Children's Bureau, U. S. Department of Labor, Washington 25, D. C. The conference, the first of its kind, was called specifically for a pooling of experience in the operation of rheumatic fever control programs by state crippled children's agencies (THE JOURNAL, Oct. 30, 1943, p. 578). It was broad in scope, providing an opportunity for a general review of medical, nursing and social problems affecting the rheumatic child. Representatives of many lay and professional groups contributed to the discussion. State rheumatic fever programs are operated by state crippled children's agencies under plans approved by the Children's Bureau and are supported in large part with funds made available under the Social Security Act. The first of these programs was initiated in Oklahoma in 1940. Today state rheumatic fever programs are in effect in nineteen states. Even in these states, however, the problem has scarcely been touched, for services are available in only 239 of the 3,082 counties in the United States and its territories. Only about $450,000 of federal funds are budgeted for these rheumatic fever programs this fiscal year, a small sum in comparison with the magnitude of the program. The bureau estimates that half a million children in the United States have or are suffering from rheumatic fever.

States Urged to Help in Public Works

Major Gen. Philip B. Fleming, federal works administrator, recently called on the states to assume a greater measure of financial responsibility for the maintenance of schools, hospitals and other public services in war impacted areas. He also directed to their attention the limited amount of Lanham act funds that remain available. In letters to the governors, General Fleming pointed out that many states have treasury surpluses. He also explained that the conditions which made necessary the facilities are likely to persist indefinitely in many areas. The state executives were advised that the Federal Works Agency would cooperate with them and with the local sponsors in working out a program mutually satisfactory and in the best interests of the people as a whole. To date the FWA has allotted $93,830,767 for maintenance and operation costs of all types of public services, including schools, hospitals, child care and recreation centers and venereal disease rapid treatment hospitals. The allotments for schools totaled $27,679,799, child care $42,048,764, venereal hospitals $12,802,165 and recreation $6,404,906. Lanham act funds now available do not permit allotments to maintain and operate new facilities except to meet an urgent emergency and are just about sufficient to help keep in operation those already established and still vitally needed. "Federal funds which may be used for these purposes are necessarily limited," General Fleming wrote the governors, "and in view of the fact that many of the states have accumulated treasury surpluses it is my sincere desire that a way may be found whereby the states and their political subdivisions will be able to assume a greater measure of financial responsibility for the maintenance of such facilities, especially since the need is likely to persist in many areas after the authority of the agency to assist is terminated. The wholehearted cooperation which this agency has received from you in the past encourages the hope that together we may arrive at a conclusion mutually satisfactory and in the best interests of the people as a whole." In an earlier letter General Fleming advised the governors of the limited amount of Lanham act funds available for school maintenance and operation. He suggested they recommend increased school appropriations to their legislatures so that the schools might not suffer undue hardship when FWA is forced to reduce, or terminate, contributions. The legislatures in most states convene this year.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 17, 1945.

The Care of Inert Patients During Transit to Base

The care of inert patients during transit to base is a problem ever present in war. The *Army Medical Department Bulletin* points out that prolonged stay in one position on a stretcher is more than uncomfortable: it may be harmful. Inert patients include those who are unconscious or paralyzed by head or spinal injuries and those who are immobilized as a result of chest or buttock wounds. Pressure sores or massive collapse of the lung are the commonest results of prolonged stay in one position; the latter appears to have a higher incidence in battle accidents than in civilian injuries. A patient who is in good condition when he starts his journey by motor ambulance or air may be found on arrival at the base to have rapid breathing and pulse and signs of a collapsed lung. In chest and buttock wounds the collapse usually occurs on the side opposite to the wound because the patient has been lying on the uninjured side so long. To prevent massive collapse of the lung and pressure sores the following precautions should be taken:

1. Before evacuation inert patients who are conscious should be given breathing exercises at regular intervals. This can be conveniently done when sulfonamide compounds are being administered. Whenever possible, inert patients for evacuation to the base should be prominently labeled "Unable to move. Please alter position during transit."

2. During transit on a stretcher, whether by motor ambulance or by air, inert patients should have their position altered slightly from time to time. Those who cannot help themselves should be placed in the lowest tier of the stretcher racks of the ambulance or plane. Once every hour the attendant should move the patient by gently lifting his pelvis into a new position. For patients with buttock wounds the lift may have to be applied to the upper part of the trunk, or the patient may be slightly rolled by altering the position of his limbs. Such movements transfer pressure to different areas of the skin and are often followed by alteration of breathing and coughing that clears the respiratory passages of mucus.

Before evacuation of patients who are paraplegic from spinal injury, each pressure point on the lower limbs (heels, malleoli, the head of each fibula) should be protected by large pads of wool and a firm bandage. Where possible an air ring should be provided for protection of the sacrum. Frequent slight alterations of the position of the limbs and trunk are essential; otherwise sloughing bed sores are inevitable. In gunshot wounds of the spine, unlike the fracture-dislocation of civil life, the spinal column is virtually intact and movement of the trunk does not produce further damage to the cord. In paraplegic patients care should be taken to ensure that the suprapubic catheter is not disturbed when the patient is moved.

3. On admission to the receiving hospital the inert patient should be promptly examined and a regimen instituted that ensures frequent change of position. Whenever possible, breathing exercises should be part of the routine.

An Industrial Health Service

A committee of the Royal College of Physicians on social and preventive medicine has presented its report on the reform of industrial medicine. As a large majority of citizens spend a third of their working days in factories, offices and other places of business, the report points out, the importance of an industrial health service is evident. An industrial health service should be planned boldly without much regard for traditional arrangements. Factory legislation should be extended to smaller industries and nonindustrial undertakings. The industrial health service should be part of the projected national health service. There should be uniform conditions of service and rates of pay. General administration might be mainly delegated to the Ministry of Labor but in special industries could be carried out by such bodies as the Ministry of Fuel and Power, the Ministry of War Transport or the General Post Office. The service should be national in its scope and apply to every variety of employment.

The service should be staffed by medical inspectors, by consultants in industrial medicine and by whole time and part time medical officers with a nonmedical personnel trained for the type of work undertaken. Clinical facilities, including beds for consultants and research workers in industrial medicine, should be provided. The aims should be promotion of the general health of the worker by providing the optimum environmental conditions, by preventing disease and accidents in industry, by taking an appropriate share in rehabilitating the disabled and by educating the workers in preserving health and well being. Research in industrial health should be given every possible encouragement. As the service is comprehensive and national in scope, the family doctor has a vital part to play in it as a part time industrial officer. He should be trained for this function.

Fitting the individual worker for his job will entail inquiry into his physical and mental capacity. The doctor's share in selection and allocation is not restricted to those entering industry but is equally necessary when workers change their occupation, perhaps because of illness. As to rehabilitation, efficient facilities for it require the closest ties between the national health and the industrial service. The final stages of restoration should be carried out at the place of work. For those who wish to take up industrial health as a career, training should be provided based on a broad study of preventive and social medicine in order to avoid too narrow specialization. A special course of instruction in industrial health should be preceded by at least two years of postgraduate experience in medicine, of which not less than one year should be spent in general practice. Whether a special diploma in industrial health is instituted or not there should be a well designed course of training of one year's duration. As to research work, up to the war the Industrial Health Research Board carried out pioneer work which promised great benefits to industrial organizations. After the war there will be increasing need for research in both field and laboratory. At present teaching schools are considering the creation of departments and chairs in industrial health.

British Medical Officer Honored by President Roosevelt

As chief surgeon of the allied forces Major General Sir Ernest Marshall Cowell planned and executed the medical services for the allied landings and subsequent operations in North Africa, Sicily and Italy. For exceptionally meritorious conduct in the performance of outstanding services from September 1942 to March 1944 as director of medical services, Allied Headquarters, Mediterranean Theater, he was decorated with the Legion of Merit by General Eisenhower, Allied Supreme Commander. The decoration was awarded by President Roosevelt. According to the citation, "by personal supervision and inspection of the forward areas, and by effecting new technics whenever necessary to meet the constantly changing situation, he welded together medical services of the American and British forces and produced a highly successful organization, which resulted in the saving of many lives and contributed to the well being and comfort of the sick and wounded of both nations."

PALESTINE

(From Our Regular Correspondent)

JERUSALEM, Feb. 2, 1945.

Endocrine Allergy

In a lecture held at the Jewish Medical Association in Jerusalem, Zondek and Bromberg submitted the results their research in the field of endocrine allergy had yielded during recent years. It is generally accepted that allergic manifestations are elicited by exogenic allergens. But there are evidences that allergic reactions may also occur following the action of endogenous allergens produced within the organism by endocrine glands. Certain pathologic disturbances are due to this peculiar reactivity of the organism to the action of its hormones and of the products of their metabolism. The name of "endocrine allergy" has been proposed for these conditions. It has been shown that this kind of allergic reactions may arise not only following the action of endogenous glandular secretions of protein nature as thyroxin, insulin and chorionic gonadotropin but also as the result of allergenic activity of steroid hormones (estradiol, progesterone, testosterone, desoxycorticosterone) and their products of metabolism (estrone, pregnandiol, androsterone). The following clinical observations point to the existence of endocrine allergy:

(*a*) In certain cases injections of estrone, estradiol benzoate or other steroid hormones induce general symptoms, such as nausea, vomiting, fever, diarrhea and urticaria.

(*b*) Certain allergic diseases (asthma, angioneurotic edema, urticaria, migraine) take sometimes a particularly severe form during the premenstrual phase in which production of the follicle and corpus luteum hormones reach maximal levels.

(*c*) In some cases of pruritus vulvae, administration of estrogenic substance gives relief only if given in low dosage; large doses may cause severe exacerbation of the disease. The successful treatment of pruritus vulvae by percutaneous application of small quantities of sex hormones (Zondek) is plausibly explained as a consequence of desensitization through continuous absorption of hormone in regular doses.

In an investigation made on a series of 32 healthy, regularly menstruating women and 150 patients complaining of various disorders suspected of being conditioned by endocrine allergy, numerous facts supporting the hypothesis of sensitivity to endogenous secretions have been established. The latter may be thus summarized:

1. The skin reagins to the steroid hormones have been demonstrated by the specific positive reaction which appears twenty-four to forty-eight hours after intracutaneous injection of a minimal quantity of hormone; analogous conditions of sensitivity to protein and insulin may occur. The positive skin reactions to hormones have been observed in women suffering from various disorders related to menstruation or the menopause but never in healthy subjects.

2. In patients sensitive to steroid hormone it is possible to reactivate the formerly positive skin reaction by subcutaneous injection of the hormone in question in another site ("recurrent reaction").

3. In some patients in whom the allergic symptoms appear in the premenstruum, the positive cutaneous reaction may recur for several months in the premenstrual period. This "retarded reaction," which appears at the same time coincident with the attainment of a maximum level in the body by the allergenic hormone, is further proof of the existence of endocrine allergy.

4. The passive transfer test (positive Prausnitz-Kuestner test) has been obtained on many occasions with serum of patients sensitive to hormones; this observation points to the presence of allergic antibodies circulating in the blood of these patients.

5. Injections of minimal quantities of glandular products into persons who have not previously received endocrine treatment may cause serious general symptoms.

6. Personal and family histories of allergy and high blood eosinophilia are frequent in persons with positive cutaneous tests.

7. Specific desensitization by injections of gradually increasing doses of allergenic hormone gave favorable clinical results in various disturbances related to the menstrual cycle or the menopause; it is a proof that the disturbances in question have been caused by endocrine allergy.

The results of this investigation lead to the assumption that in patients showing allergic manifestations attention should be paid not only to the exogenic allergens but also to the possibility of sensitivity to endogenous hormones. These facts should be kept in mind in the study of various clinical pictures and their differential diagnosis. It has been shown that certain disturbances related to the menstrual cycle, as premenstrual tension, migraine, urticaria, pruritus vulvae, premenstrual fever and certain ocular manifestations (superficial keratitis), often result from allergy to endogenous hormones. On the other hand, various complaints appearing at the menopause as migraine and pruritus vulvae may also be due to endocrine allergy. Certain cases of asthma, vasomotor rhinitis and angioneurotic edema presenting a particularly severe course during the premenstrual phase or the menopause may also be caused by this peculiar kind of allergic sensitivity. The fact that the organism may react allergically to secretions of its own endocrine glands throws a new light on the study of allergy.

Marriages

GEORGE ALFRED HIGGINS JR., Albuquerque, N. M., to Miss Isabelle Jeannette Heck of Chicago in Rochester, Minn., January 23.

RICHARD CAMPBELL CLAY, Birmingham, Ala., to Miss Madeline Murray of Whalesville, Md., in Baltimore, December 30.

GRANVILLE ALLEN LAWRENCE JR., Philadelphia, to Miss Rebecca Belle Patterson of Hollidaysburg, Pa., November 17.

ANTHONY M. KURLAND, Denver, to Miss Lucille Elizabeth Theraux of Philadelphia in Fairfield, Ohio, December 1.

WILLIAM NYE CORPENING, Houston, Texas, to Miss Avis Simons Kiser, formerly of Laurens, S. C., December 23.

HENRY BERNARD STRYKER JR., Englewood, N. J., to Miss Carolyn Roberta Guy of Glens Falls, N. Y., December 2.

GUS EVANS FORBES JR., Greenville, N. C., to Miss Nancy Burnette Armistead of South Hill, Va., November 25.

JOHN DAVID FOLSOM to Miss Ruth Corinne Ludwick, both of Lincoln, Neb., in Staten Island, N. Y., January 20.

WALTER MACINTIRE WHITEHOUSE, Ypsilanti, Mich., to Miss Barbara Norton McIntyre of Grand Rapids recently.

KEARNS REID THOMPSON JR., Durham, N. C., to Miss Sara Elizabeth Bell of Dillon, S. C., December 30.

ARTHUR RHETT GUNTER, Rock Hill, S. C., to Miss Emily Sims Jennings of Spartanburg, December 16.

CHARLES ROBERT WATSON to Miss Pauline Lindsey Davis, both of Little Rock, Ark., December 26.

JOHN W. DONNELL, Hudson, Iowa, to Mrs. Ruth Lowell of Fort Lauderdale, Fla., October 1.

RAYMOND ROBERT SUSKIND to Miss Ida Blanche Richardson, both of New York, December 27.

SAMUEL C. MURPHY to Miss Hazel Jamison Melick, both of Warsaw, Ind., January 9.

HUGO J. EHRENFELD to Miss Eve Emerson Pauker, both of New York, January 27.

HAROLD M. GOODMAN to Miss Harriett Lewis, both of Richmond, Va., December 3.

THOMAS V. BANKS to Miss Jean Sorrell, both of Dyersburg, Tenn., January 7.

Deaths

Sara Josephine Baker ✠ Bellemead, N. J.; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1898; in 1901 joined the New York City Department of Health as a school medical inspector; six years later appointed assistant to the health commissioner, serving until 1908, when she became director of the newly organized bureau of child hygiene of the New York City Department of Health, which was the first of its kind under governmental control and which was eventually copied by some thirty-five states; resigned from that position in 1923; for many years lecturer on child hygiene at Columbia and New York universities; formerly consultant in child hygiene to the U. S. Public Health Service and a member of the Health Committee of the League of Nations; consultant to the Children's Bureau, U. S. Department of Labor; member of the New Jersey State Board of Health; member of the medical board of the Maternity Center Association, New York City; member of the board and consulting pediatrician to the Clinton (N. J.) Reformatory for Women; fellow of the New York Academy of Medicine and the American Public Health Association; member of the Medical Society of the State of New York; honorary member of the Medical Society of the State of New Jersey and the Somerset County Medical Society; associate member of the American Academy of Pediatrics; member and past president of the Medical Women's National Association; past president of the American Child Hygiene Association; honorary president of the Children's Welfare Federation of New York City; member of the board of trustees of the New York Infirmary for Women and Children; in 1917 received the degree of doctor of public health from the Bellevue Hospital Medical College, New York; lectured extensively in this country and in Europe; in the years 1939 and 1940, the American Woman's Suffrage Association and the General Federation of Women's Clubs (in connection with their fiftieth anniversaries) and the Congress of Women of the World's Fair bestowed on her recognition of her achievement in the field of public health as one of the outstanding fifty women of this country; author of "Healthy Mothers," "Healthy Babies," "Healthy Children," "Child Hygiene" and an autobiography, "Fighting for Life"; died in New York Hospital February 22, aged 71.

Ellice Murdoch Alger ✠ New York; University of Vermont College of Medicine, Burlington, 1893; specialist certified by the American Board of Ophthalmology; for many years professor of ophthalmology and clinical ophthalmology at the New York Post-Graduate Medical School, Columbia University, and surgeon at its hospital; at one time taught at his alma mater; one of the founders in 1915 of the National Society for the Prevention of Blindness, serving continuously on its board of directors until his death; at one time a member of the subcommittee for the prevention of blindness organized by the New York Association for the Blind; in 1938 the Association for Research in Ophthalmology, of which he was a member, in cooperation with the St. Louis Society for the Blind, awarded him the Leslie Dana Gold Medal for "outstanding achievements in the prevention of blindness and the conservation of vision"; member of the American Ophthalmological Society and the New York Ophthalmological Society, of which he was past president; served as chairman of the section of ophthalmology of the New York Academy of Medicine; fellow of the American College of Surgeons; author of "Refraction and Motility of Eye"; died in the New York Post-Graduate Hospital February 18, aged 74.

Byron McBride Caples ✠ Waukesha, Wis.; Willamette University Medical Department, Salem, 1889; Rush Medical College, Chicago, 1891; member of the House of Delegates of the American Medical Association in 1905, 1906, 1907, 1908 and 1911; past president of the State Medical Society of Wisconsin; twice president of the Waukesha County Medical Society and in 1943, in recognition of his completion of fifty years in the practice of medicine, awarded honorary life membership in the society; in 1924 president of the Milwaukee Neuro-Psychiatric Society; member of the American Psychiatric Association, Milwaukee Academy of Medicine, Medical Veterans of the World War, National Geographic Society and State Historical Society of Wisconsin as well as the Waukesha Chamber of Commerce; during World War I served as chairman of the medical advisory board of Waukesha County, also serving on the Waukesha council of defense and as psychoneurologist on the draft board; in 1898 established the Waukesha Springs Sanitarium and operated it until 1943, when the largest building on the property was sold to Carroll College, named Caples Hall in his honor; died in the Waukesha Memorial Hospital January 18, aged 84.

Robert Ratze Brown ✠ Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1914; assistant professor of clinical orthopedic surgery at his alma mater; a member of the board of directors and past president of the Nashville Academy of Medicine; past president of the Davidson County Medical Society; member of the American Proctologic Society, Clinical Orthopedic Society, Southern Medical Association and the American Academy of Orthopaedic Surgeons; specialist certified by the American Board of Orthopaedic Surgery; a captain with the Vanderbilt medical unit attached to the First Division during World War I; on the staffs of the Vanderbilt, St. Thomas, Protestant and Nashville General hospitals; member of the Tennessee State Crippled Children Commission and had been active in the medical work of the Junior League Home for Crippled Children for many years; died February 6, aged 54, of coronary thrombosis.

Shenton Stanley King ✠ New Rochelle, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1905; member of the American Psychiatric Association and the American Orthopsychiatric Association; fellow of the Royal Institute of Public Health, London; received many decorations for his services during World War I; since 1933 a member of the bureau of child guidance, department of family and child welfare of Westchester County; served on the staff of the Grasslands Hospital, Valhalla; received the doctor of public health degree from Johns Hopkins University School of Hygiene and Public Health in Baltimore in 1924; died in the New Rochelle Hospital January 4, aged 66, of cerebral hemorrhage.

James Harold Mathews ✠ Seattle; University of Michigan Medical School, Ann Arbor, 1922; president-elect of the King County Medical Society; formerly instructor of otolaryngology at his alma mater; specialist certified by the American Board of Otolaryngology; member of the Pacific Coast Oto-Ophthalmological Society; served as president of the Puget Sound Eye and Ear Society; interned at the Harper Hospital in Detroit; president of the Seattle Eye, Ear, Nose and Throat Infirmary; on the attending staff of the Swedish Hospital; consultant on the staffs of the Children's Orthopedic Hospital and the Providence Hospital, where he died January 30, aged 49, of heart block during cholecystectomy and aortic insufficiency.

William Harry Barnes ✠ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1912; specialist certified by the American Board of Otolaryngology; served as lecturer on bronchoscopy at Howard University and consulting bronchoscopist at Freedmen's Hospital, both in Washington, D. C.; assistant surgeon in the U. S. Public Health Service during World War I; member and assistant treasurer of the Philadelphia Housing Authority; on the staffs of the Jefferson Hospital and the Mercy Hospital, where he died January 15, aged 57, of transverse lesion of the cord incurred from an injury.

Anthony Barone, Boston; Middlesex College of Medicine and Surgery, Cambridge, 1921; member of the American Medical Association; also a dentist and pharmacist; died December 8, aged 48, of bronchopneumonia.

Frank Burr Combs, Chicago; Northwestern University Medical School, Chicago, 1905; member of the American Medical Association; died in the Albert Merritt Billings Hospital January 20, aged 65, of coronary thrombosis.

Charles H. Donoho, Portland, Tenn.; University of Nashville Medical Department, 1899; member of the American Medical Association; died in St. Thomas Hospital, Nashville, December 2, aged 71.

Albert George Kreimer, Cincinnati; University of Cincinnati College of Medicine, 1922; member of the American Medical Association; died in the Mercy Hospital December 22, aged 50.

William John Reed, Peoria, Ill.; University of Illinois College of Medicine, Chicago, 1934; died in Los Angeles December 9, aged 35.

Eugene Clyde Underwood Jr., Louisville, Ky.; Hospital College of Medicine, Louisville, 1904; examiner for the Reynolds Research Corporation; served on the staff of SS Mary and Elizabeth Hospital, where he died December 30, aged 62, of coronary thrombosis.

William R. Washburn, Fort Bayard, N. M.; St. Louis University School of Medicine, 1904; member of the American Medical Association; served during World War I; served on the staff of the Veterans Administration Facility, where he died December 28, aged 68, of coronary arteriosclerotic heart disease.

Frank W. Watson, Union City, Tenn.; Missouri Medical College, St. Louis, 1885; past president and secretary of the Obion County Medical Society; served on the school board; died in the Union City Clinic January 2, aged 81, of pneumonia.

DIED WHILE IN MILITARY SERVICE

Patrick Sarsfield Haran, Brooklyn; Long Island College Hospital, Brooklyn, 1923; member of the American Medical Association; served on the staffs of the Kings County, Holy Family and Midwood hospitals; commissioned a captain in the medical corps, Army of the United States, on Aug. 18, 1942; died in the Regional Hospital, Fort Jay, N. Y., Dec. 15, 1944, aged 46, of epidemic infectious hepatitis and bronchopneumonia.

Edward Thorne Harrison, High Point, N. C.; University of Virginia Department of Medicine, Charlottesville, 1926; fellow of the American College of Surgeons; member of the American Medical Association; interned at the Battle Creek Hospital, Battle Creek, Iowa, Jamaica Hospital, Richmond Hill, N. Y., Chesapeake and Ohio Railway Hospital, Clifton Forge, Va., and the Willard Parker Hospital in New York; member of the surgical staff of the Burrus Memorial Hospital; commissioned a major in the medical corps, Army of the United States, on July 18, 1942; died in the Moore General Hospital, Swannanoa, Dec. 18, 1944, aged 46, of aplastic anemia.

John Milton Hill ✠ Pittsburgh; University of Pittsburgh School of Medicine, 1932; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America, Inc., and the American College of Radiology; served on the staffs of the Passavant, St. John's General, Presbyterian and Woman's hospitals; assistant radiologist at the Falk Clinic; commissioned a major in the medical reserve corps of the U. S. Army on April 13, 1942; began active duty on July 15, 1942; stationed at Fort Lewis, Wash., with the Pitt Medical Unit until December 1943, when he was sent to Australia with Base Hospital unit number 27; promoted to lieutenant colonel; died in the Walter Reed General Hospital, Washington, D. C., November 13, aged 46, following an operation for brain tumor.

George Forster Hilles, Cleveland Heights, Ohio; Western Reserve University School of Medicine, Cleveland, 1939; interned at St. Vincent Charity Hospital and served a residency in medicine at the Evangelical Deaconess Hospital in Cleveland; commissioned a lieutenant in the medical reserve corps of the U. S. Army, June 14, 1939; began active duty in the Army of the United States on May 5, 1941; later promoted to captain; after serving nineteen months in Panama, returned to the United States in April 1943; subsequently went to North Africa and Italy, where he was killed in an airplane accident Aug. 23, 1944, aged 30.

James Willard McMurray, Williston, Fla.; Tulane University of Louisiana School of Medicine, New Orleans, 1934; member of the American Medical Association; health officer of Gilchrist-Levy Counties Health Department; formerly district health officer of West Florida with headquarters at Marianna, director of the Broward County Health unit with headquarters at Fort Lauderdale, and the Gulf-Calhoun-Franklin unit with headquarters at Apalachicola; commissioned a first lieutenant, medical corps, Army of the United States, on March 3, 1944; died in the Billings General Hospital, Fort Benjamin Harrison, Ind., Dec. 14, 1944, aged 38, of coronary occlusion.

Oscar Frederick Nolan ✠ San Francisco; Baylor University College of Medicine, Dallas, 1927; specialist certified by the American Board of Urology, Inc.; member of the Pacific Association of Railway Surgeons and the Western Branch of the American Urological Association; urologist for the Southern Pacific Hospital and St. Francis Hospital; consulting urologist at the French Hospital; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on May 30, 1927; began active duty as a captain in the Army of the United States on July 27, 1941, stationed at the Letterman General Hospital, where he was chief of the urologic service; later promoted to major and lieutenant colonel; accidentally drowned in the Abbotts Lagoon, Marin County, while duck hunting, Nov. 12, 1944, aged 44.

Joe Holmes Price, Poplarville, Miss.; University of Oklahoma School of Medicine, Oklahoma City, 1928; served during World War I; formerly on the staffs of various Veterans Administration facilities; at one time state district health superintendent at McLeansboro, Ill.; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on Feb. 12, 1930; began active duty as a captain in the Army of the United States on July 22, 1942; died 5 miles East of Baton Rouge, La., Dec. 4, 1944, aged 46, of injuries received in an automobile accident.

Raphael Raymond Sprafka ✠ Chicago; Northwestern University Medical School, Chicago, 1937; interned at the Hospital of St. Anthony de Padua; diplomate of the National Board of Medical Examiners; commissioned a first lieutenant in the medical corps, Army of the United States, on Aug. 3, 1942; promoted to captain on Oct. 5, 1943; died in Beauvais Tille, France, Dec. 4, 1944, aged 33, of multiple fractures incurred in an airplane crash.

Judson Ludwell Taylor ✠ Commander (MC), U. S. Navy, retired, Houston, Texas; University of Texas School of Medicine, Galveston, 1903; professor and chairman of the department of surgery at Baylor University College of Medicine; served as professor of general and oral surgery at the Texas Dental College from 1931 to 1943, when he became supervisor of hospital instruction at the University of Texas School of Dentistry, from which position he resigned to accept an appointment by the governor of Texas to the board of regents of the University of Texas, Nov. 15, 1944; served as lecturer in surgery at his alma mater; president of the State Medical Association of Texas, 1942-1943, and councilor of the Ninth District from 1939 to 1941; president of the Harris County Medical Society in 1934; founder member of the American Board of Surgery; member of the Texas Surgical Society, American Association for the Surgery of Trauma, Association of Military Surgeons of the United States, History of Science Society and the Southern Medical Association; fellow of the American College of Surgeons; served as trustee of the Houston Academy of Medicine; chief surgeon at the Southern Pacific Hospital; consulting surgeon, Jefferson Davis, Memorial and the Methodist hospitals; surgeon in chief, Hermann Hospital; appointed chief of staff of the Arabia Temple's Crippled Children's Hospital in 1922, becoming chief of staff emeritus in 1930; recently surgeon to the M. D. Anderson Hospital for Cancer Research, president of the Maternal Health Center from 1936 to 1943, medical director of the Birth Control League of Texas from 1938 to 1941 and the Texas League for Planned Parenthood from 1941 to 1943; a member of the executive committee, Harris County chapter, National Foundation for Infantile Paralysis, since 1943; served as member of the board of directors of the Union National Bank; appointed assistant surgeon in the U. S. Navy on Jan. 17, 1904 and retired on Feb. 19, 1912 for incapacity resulting from an incident of service; awarded the Victory Medal for his services during World War I, for which he had been recalled to active duty as a lieutenant commander in the U. S. Navy; in June 1942 recalled to active duty with rank of lieutenant commander; on Sept. 22, 1943 was given a spot promotion to the rank of commander, medical corps, U. S. Navy, retired, the rank held at the time of his death; senior medical officer in the office of naval officer procurement; died Nov. 28, 1944, aged 63, of coronary occlusion.

Charles Edward Walker Jr., Denver; Harvard Medical School, Boston, 1932; member of the American Medical Association; interned at St. Luke's Hospital, Denver; served a residency in ophthalmology at the Massachusetts Eye and Ear Infirmary, Boston; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; specialist certified by the American Board of Ophthalmology; formerly instructor in ophthalmology at the University of Colorado School of Medicine; served on the staffs of St. Luke's, Colorado General, Denver General, St. Joseph's and Presbyterian hospitals; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on June 23, 1932; began active duty as a captain on Feb. 6, 1941; later promoted to major and lieutenant colonel; died in Paris, France, Nov. 22, 1944, aged 41, of coronary occlusion.

Correspondence

WILL PENICILLIN BE USED INDISCRIMINATELY?

To the Editor:—Penicillin will soon be available for general civilian use. It is understood that commercial firms will soon have sufficient supplies to market it through their usual channels and that it will soon reach the local drugstore. There it will almost certainly be available to the general practitioner on much the same basis as any other biologic product. While still expensive, its price will not be prohibitive. Its use will in all likelihood be widespread, both because of its remarkable efficacy and because of the magic of its name to doctor and public alike. Further, the recent announcement by Libby (*Science,* February 16) that penicillin in cottonseed oil solution enclosed in gelatin capsules has been satisfactorily administered by mouth to human beings appears to herald even more extensive use of penicillin and its related compounds.

It would seem that now is the time to take proper safeguards against their indiscriminate use. The proper patterns, set now, might well avoid the tragedies that accompanied the introduction of the sulfonamide drugs and the waste that accompanied the introduction of purified vitamin preparations.

Time alone will tell what the abuses of penicillin are to be. Its parenteral administration has resulted in an infrequent but definite number of reactions such as urticaria (see Report of the Committee on Chemotherapeutic and Other Agents of the National Research Council in THE JOURNAL, Aug. 28, 1943, page 1217, and other reports), thrombophlebitis and even contact dermatitis (Pyle, H. D., and Rattner, Herbert, *ibid.,* July 29, 1944, p. 903). Penicillin may be harmful in acute rheumatic fever (Foster, F. P., and others, Sept. 30, 1944, p. 281) and penicillin resistant strains may develop (Virulence of Penicillin Resistant Bacteria, editorial, Aug. 12, 1944, p. 1042). It is not yet fully known how many of the reactions described were due to impurities in the penicillin preparations then in use, nor is there much information about the toxic reactions, or their lack of them, with penicillin taken by mouth in a vehicle suitable for its ultimate absorption. Penicillin so far appears to be a far safer drug than the sulfonamides, and its indiscriminate use might actually be accompanied by fewer reactions than with the current widespread consumption of aspirin or by less economic waste than now accompanies the indiscriminate use of purified vitamins.

Pehaps the greatest danger of the indiscriminate use of penicillin is of another sort, namely the development of a sense of false security. Penicillin is of no use in many diseases, and in others there is danger from inadequate dosage. For example, it is not hard to visualize that a patient with a chancre would hear that penicillin cures syphilis, would get hold of some, take it (or have it administered) in inadequate dosage, see his chancre disappear, feel that he has been cured of the disease, and then develop cerebrospinal or cardiovascular syphilis many years hence. Numerous other examples can be imagined, and some have probably already occurred.

Nor does it appear unlikely that a period of commercial exploitation of penicillin will soon set in. It is not at all unlikely that the "patent medicine" manufacturers will soon get hold of the drug and we may soon have intense salesmanship of penicillin chewing gum, penicillin cough drops and penicillin mouth wash, not to mention penicillin skin cream or even penicillin laxatives. Perhaps such mild unleashings of the imagination will prove to be too conservative.

It is certainly too early to know yet just how the matter will develop. It would appear to be none too early, however, to reassure ourselves of at least the following:

1. That adequate research will be undertaken, and maintained, to ascertain the best forms of penicillin and related compounds for therapeutic use, their indications and contraindications, their best routes of administration and their toxic reactions, both direct and indirect.

2. That adequate education of the doctor, the druggist and the public will be carried on to assure the proper use (and restraint from use) of penicillin.

3. That proper steps will be taken by professional organizations, particularly the medical and pharmaceutical associations, to prevent possible abuses of penicillin and to assure its availability where needed.

4. That the drug industry will take the necessary steps to foresee and prevent, mainly through voluntary discipline, possible abuses and maldistribution.

5. That the government will not relax its controls until there is evidence that to do so would not lead to shortages in cases in which penicillin is necessary or, contrarywise, to a riot of commercialized penicillinization of our population.

Some of the points of view in this communication may be mistaken, especially since I am no longer intimately associated with work on penicillin (my former contact was outlined in a previous communication in THE JOURNAL, April 22, 1944, p. 1219). There are quite clearly dangers from the failure to use penicillin in disease which it alone will cure. There are also dangers of too stringent controls on its use. These are not discussed here, since the opposite factors appear to need more emphasis now. It would appear that full discussion of this question, perhaps mainly in the columns of THE JOURNAL, would be of considerable importance in avoiding mistakes which might prove tragic as penicillin becomes more readily available. Penicillin has got off to a good start under the guidance of the O. S. R. D., the National Research Council and the W. P. B. It would be sad if its future was less wholesome.

LESLIE A. FALK, 1st Lieutenant, M. C., A. U. S.

To the Editor:—The public press announces a wide range of applications of penicillin in preparation for release to laymen after March 15. Penicillin lozenges, chewing gum and dental paste are listed with penicillin vaginal jelly. Further, it is stated that cosmetic manufacturers are studying penicillin with an eye toward including penicillin in face creams, shaving pastes and lotions and similar products.

What measures, if any, have been taken to control the self administration of penicillin in the vehicles listed? Has any official representation been made to the Food, Drug and Cosmetic Administration regarding need for regulation? Has any state or municipality amended its sanitary code or pharmacy laws to include penicillin? Has any official educational effort been initiated to apprise the potential customers of penicillin toothpaste, penicillin dental cream or penicillin chewing gum regarding the effective time-dose factors for effective utilization of the drug? Inadequate dosage is now known to mask the symptoms of syphilis when administered for gonorrhea. It is not too much to expect that partial indiscriminate dosage of penicillin through self administration by throat lozenges, chewing gum, shaving cream and vaginal jellies will produce other examples to the detriment of the sick and the formation of a large army of infection carriers.

The time is now to make the proper moves—now while penicillin is still restricted in distribution.

HERMAN GOODMAN, M.D., New York.

SULFADIAZINE IN PREVENTION OF MENINGITIS

To the Editor:—It may be of interest, particularly to physicians in mental hospitals, to be informed of a situation which developed at this institution, and the procedure adopted.

On Nov. 12, 1944 a man aged 33 whose mental diagnosis was psychosis with organic changes of the central nervous system, paralysis agitans, was given a clinical diagnosis of cerebrospinal meningococcic meningitis, which was directly confirmed by laboratory examinations. Penicillin was given intrathecally, with definite improvement manifest the following day, and he made a prompt and uncomplicated recovery, receiving two subsequent doses of penicillin.

The point of interest is this: The patient was located in a very crowded ward. It seemed inevitable that many of the 400 patients and personnel in this ward had been exposed. Following the technic described in an article by Lieut. Col. Joseph F. Painton, M. C., U. S. Army, published in the October 1944 issue of the *Military Surgeon* on page 267, all 400 received 2 Gm. of sulfadiazine by mouth, followed in six hours by a second dose of 2 Gm. and a third dose of 1 Gm. given twelve hours after the second dose. No further cases developed, and no ill effects were observed from these prophylactic doses.

The apparent results of this procedure would appear to be significant and worth trying in institutions where overcrowding is as serious as it is in many instances today.

CHARLES A. ZELLER, M.D., Philadelphia.
Superintendent, Philadelphia State Hospital.

TREATMENT OF HYPERTHYROIDISM WITH THIOURACIL

To the Editor:—In a recent editorial (THE JOURNAL, February 10, p. 334) commenting on British experience in the treatment of hyperthyroidism with thiouracil as reported by Nussey in the *British Medical Journal*, Dec. 9, 1944, it is remarked that this author has apparently presented a safe basis for continued administration of thiouracil. It is suggested that 0.6 Gm. daily of thiouracil be administered daily for three to five weeks with gradual reduction thereafter to the minimal effective dose. Adequate supervision of the patient is urged without definition of this phrase. No mention is made of any toxic reactions.

Analysis of Nussey's article shows that there were 27 patients treated for periods varying from three weeks to twelve months with dosages ranging from 0.05 to 0.6 Gm. daily. Observations included leukocyte counts at intervals of one to several months. Among the 27 patients there were 4 with skin eruptions. Seven of the 27 patients exhibited either neutropenia or leukopenia during treatment. It is significant that many of the low counts occurred after the basal metabolic rate had become normal. The author himself notes that "consistently low figures were seen" in 2 cases. No serious neutropenic reactions occurred in this series, but in almost all published series at least one severe neutropenic or agranulocytic reaction has been observed, occasionally with fatality. Our own experience with the use of thiouracil in the treatment of toxic goiter has confirmed these findings. Those who employ thiouracil should "adequately supervise" its administration by performing leukocyte counts at least three times weekly, with differential counts whenever the total count drops below 5,000 per cubic millimeter. In addition, our experience, as well as that of others, has demonstrated the importance of frequent clinical observation with respect to skin eruptions, pharyngitis, fever and jaundice. Moreover, there is considerable evidence that the dosage-time factor is not of determining significance in the development of toxic reactions to the drug.

SAMUEL L. GARGILL, M.D.
MARK FALCON LESSES, M.D.
Boston.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, March 10, page 614.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery 4.

ALASKA: Juneau, March. Sec., Dr. W. M. Whitehead, Box 561, Juneau.

ARIZONA: * Phoenix, April 3-4. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Eclectic.* Little Rock, June 7. Sec., Dr. C. H. Young, 1415 Main St., Little Rock. *Medical.* Little Rock, June 7-8. Sec., Dr. D. L. Owens, 701 Main St., Little Rock.

CALIFORNIA: *Oral.* San Francisco, May 20. *Written.* San Francisco, July 9-12. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

COLORADO: * Denver, April 3-6. Final date for filing application is March 19. Sec., Dr. J. B. Davis, 831 Republic Bldg., Denver.

CONNECTICUT: * *Endorsement.* March 27. Sec., to the Board, Dr. Creighton Barker, 258 Church St., New Haven.

DELAWARE: *Examination.* Dover, July 10-12. *Reciprocity.* Dover, July 17. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.

FLORIDA: * Jacksonville, June 25-26. Sec., Dr. Harold D. Van Schaick, 2736 S. W. Seventh Ave., Miami 36.

IDAHO: Boise, July 10. Dir., Bureau of Occupational Licenses, Miss Agnes Barnhart, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, April 3-5. Superintendent of Registration, Department of Registration and Education, Mr. Philip Harmah, Springfield.

INDIANA: Indianapolis, Aug. 28-30. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis 4.

KENTUCKY: Louisville, June 18-20. Sec., State Board of Health, Dr. Philip E. Blackerby, 620 S. Third St., Louisville 2.

MARYLAND: *Medical.* Baltimore, June 19-20. Sec., Dr. J. T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 19-20. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MINNESOTA: * Minneapolis, April 17-19. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: Helena, April 2-4. Sec., Dr. O. G. Klein, First Nat'l. Bank Bldg., Helena.

NEW JERSEY: Trenton, June 19-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 9-10. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NORTH DAKOTA: Grand Forks, July 3. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Endorsement.* Columbus, April. Columbus, June. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, June 14-16. Sec., Dr. J. D. Osborn, Jr., Frederick.

PENNSYLVANIA: April 10-13. Act. Sec., Bureau of Professional Licensing, Department of Public Instruction, Mrs. M. G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, April 5-6. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 25-27. Sec., Dr. N. B. Heyward, 1329 Blandina St., Columbia.

SOUTH DAKOTA: * Pierre, July 17-18. Sec., Medical Licensure, State Board of Health, Dr. Gilbert Cottam, State Capitol, Pierre.

TEXAS: Galveston, June 4-6. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

VERMONT: Burlington, June. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: * Richmond, June 20-23. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WASHINGTON: * Seattle, July 16-18. Sec., Department of Licenses, Miss Nell Adams, Olympia.

WISCONSIN: * Milwaukee, June 26-28. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: June 9. Address State Board of Healing Arts, 250 Church St., New Haven 10.

DISTRICT OF COLUMBIA: Washington, April 23-24. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington 1.

FLORIDA: DeLand, June 1. Final date for filing application is May 17. Sec., Dr. J. F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, April 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor and Detroit, May 11-12. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

MINNESOTA: Minneapolis, April 3-4. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis 14.

NEBRASKA: Omaha, May 1-2. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: Oklahoma City, April 9. Sec., Dr. J. D. Osborn, Jr., Frederick.

SOUTH DAKOTA: Yankton, June 19. Sec., Dr. G. M. Evans, Yankton.

TENNESSEE: Memphis, March 27-28. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

WISCONSIN: Madison, April 7. Sec., Professor R. N. Bauer, 152 W. Wisconsin Ave., Room 834, Milwaukee 3.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1935 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Ophthalmology, Cincinnati

27:1339-1466 (Dec.) 1944

Obstruction of Central Retinal Vein: Clinicohistopathologic Analysis. Bertha A. Klein.—p. 1339.
Bilateral Metastatic Carcinoma of Choroid with X-Ray Therapy to One Eye: Report of Case. F. C. Cordes.—p. 1355.
Notes on Operation for Glaucoma. R. J. Masters.—p. 1371.
Amblyopia in Cases of Reading Failure. T. H. Eames.—p. 1374.
Angiodiathermy of Long Posterior Ciliary Arteries and Its Use in Treatment of Glaucoma. D. Guerry III.—p. 1376.
Production of Lens Sensitivity in Rabbits by Brucella Infection. E. L. Burky.—p. 1394.
Ophthalmoscopic Classification of Hypertensive Diseases. G. E. Clay and M. Baird.—p. 1396.
Keratoconus Posticus Circumscriptus: Case Report. G. Wise.—p. 1406.
Clinical Studies in Angiospasm. I. Givner.—p. 1408.
Frequency of Squint. M. Olive Boyle.—p. 1413.
Essential Requirements for Good Orthoptic Department. D. Dicke.—p. 1417.
Precautions Necessary in Orthoptic Training. L. B. Drye.—p. 1422.

American Journal of Physiology, Baltimore

142:633-757 (Dec.) 1944

Modified Spontaneous Activity Rhythms in Rats. L. G. Browman.—p. 633.
Relation of Adrenalin and of Carotid Sinus to Hyperglycemia of Shock. E. Mylon, C. W. Cashman and M. C. Winternitz.—p. 638.
Renal Reabsorptive Mechanism for Inorganic Phosphate in Normal and Acidotic Dogs. R. F. Pitts and R. S. Alexander.—p. 648.
Spontaneous Activity in Relation to Diet in Albino Rat. Erma A. Smith and R. M. Couger.—p. 663.
Experimental Chronic Hypertension in Rabbit. A. Grollman.—p. 666.
Filtration Across Vascular Wall as a Function of Several Physical Factors. C. Hyman.—p. 671.
Mechanism of Effect of Hyperthyroidism on Cardiac Glycogen. L. E. Moses.—p. 686.
Oxygen Tension of Arterial Blood and Alveolar Air in Normal Human Subjects. J. H. Comroe and R. D. Dripps Jr.—p. 700.
Factors Affecting Determination of Oxygen Capacity, Content and Pressure in Human Arterial Blood. F. J. W. Roughton, R. C. Darling and W. S. Root.—p. 708.
Influence of Dying Gasps, Yawns and Sighs on Blood Pressure and Blood Flow. R. A. Woodbury and B. E. Abreu.—p. 721.
Hemoglobin Concentrations, Red Cell Counts and Erythrocyte Volumes of College Women of North Central States. Margaret A. Ohlson, Dena Cederquist, Eva G. Donelson, Ruth M. Leverton, Gladys K. Lewis, Williamina A. Himwich and May S. Reynolds.—p. 727.
*Affinity of Hemoglobin for Oxygen at Sea Level and at High Altitudes. H. Aste-Salazar and A. Hurtado.—p. 733.
Improved Measurement of Effect of Intravenously Injected Adrenalin on Respiratory Exchange by Colorimetric Determination of Carbon Dioxide in Expired Air and Continuous Graphic Registration of Oxygen Consumption. R. J. Jones and F. R. Griffith Jr.—p. 744.

Affinity of Hemoglobin for Oxygen at Sea Level and at High Altitudes.—Aste-Salazar and Hurtado determined the position of the oxygen dissociation curve in arterial blood obtained from 17 healthy adult men living at sea level and from 12 Indian native residents of Morococha (Peru) at an altitude of 4,540 meters (14,890 feet). The same determination was repeated on 12 subjects of the first group within the first two hours after arrival at a high altitude and on 8 men of the second group also within the first two hours after arrival at sea level. The results were compared with those obtained in previous investigations. There seems to be enough evidence to conclude that in human beings, newcomers or residents, at altitudes of about 4,000 meters, or higher, there is no increased affinity of the blood hemoglobin for oxygen. On the contrary, the findings indicate a slight tendency toward a lower affinity, both at arterial p_H and a standard p_H of 7.40, especially in the native residents. This right shift in the oxygen dissociation curve at high altitude may be interpreted as a favorable compensatory adjustment to the low pressure environment.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

52:571-684 (Dec.) 1944

Dilatation of Vertebral Canal Associated with Congenital Anomalies of Spinal Cord. A. E. Walker.—p. 571.
Clinical and Roentgen Manifestations of Dissecting Aneurysm of Aorta. M. Ritvo and P. J. Votta.—p. 583.
Prepyloric Diverticulum of Stomach Demonstrable Only by Pressure Roentgenograms: Report of Case. A. F. Hunter.—p. 595.
Megaesophagus as Cause of Mediastinal Widening. A Hurst and S. Bassin.—p. 598.
Unusual Type of Inversion of Stomach Associated with Diaphragmatic Eventration and Other Anomalies. D. H. Rosenfeld.—p. 607.
*Lesions of Diaphragm, with Special Reference to Eventration and Report of 3 Cases. R. E. Kinzer and J. C. Cook.—p. 611.
Patent Urachus. R. W. Nichols and R. M. Lowman.—p. 615.
Dyschondroplasia with Hemangiomata (Maffucci's Syndrome): Case Report. G. R. Krause.—p. 620.
Present Value of Roentgenology in Diagnosis of Appendicitis. G. E. Gomez.—p. 624.
Roentgen Diagnosis of Incipient Cancer of Rectum. A. Oppenheimer.—p. 637.
Clinical and Roentgen Aspects of Irradiation Stricture of Rectum and Sigmoid: Its Course and Treatment. Harriet C. McIntosh and J. E. Hutton.—p. 647.

Lesions of Diaphragm.—Kinzer and Cook report 38 cases of diaphragmatic lesions found during the examination of 412,149 chest roentgenograms. Of these only 3 were considered from the roentgenologic standpoint alone to be true diaphragmatic hernias. The first of these was a congenital absence of the posterior portion of the left diaphragm. The stomach, splenic flexure of the colon and several loops of small intestine were herniated into the thoracic cavity. The second was a congenital hernia through the right foramen of Morgagni. The third was a traumatic hernia through the left hemidiaphragm following an inflammatory necrosis. The remaining 35 cases were congenital eventrations of the diaphragm, 30 occurring on the left and 5 on the right side. The authors present roentgenograms of 3 instances of congenital eventration of the right diaphragm.

Annals of Internal Medicine, Lancaster, Pa.

21:937-1092 (Dec.) 1944

*High Fluid Intake in Management of Edema, Especially Cardiac Edema: II. Clinical Observations and Data. F. R. Schemm.—p. 937.
Leukocyte Count in Primary Atypical Pneumonia of Undetermined Etiology. O. O. Meyer and Ethel W. Thewlis.—p. 997.
*Use of Benzedrine Sulfate in Obesity. F. K. Albrecht.—p. 983.
Migraine Headache: Some Clinical Observations on Vascular Mechanism and Its Control. M. Atkinson.—p. 990.
Spontaneous Mediastinal Emphysema. H. Miller.—p. 998.
*Spontaneous Pneumothorax: Report of 3 Unusual Cases. A. Goldman and H. Roth.—p. 1011.
Lupus Erythematosus (Erythematodes) and Ovarian Function: Observations on Possible Relationship, with Report of 6 Cases. E. Rose and D. M. Pillsbury.—p. 1022.

High Fluid Intake in Management of Edema.—Schemm reports clinical studies on patients who had either severe edema or advanced cardiovascular disease. Treatment consisted in giving large amounts of water orally or by vein and a "neutral" diet to insure reduced amounts of salt and sodium and a slight excess of acid ash. Small amounts of acid drugs were usually given to augment the effect of the diet. If the patient's condition permitted, digitalis, mercurial diuretics and even acid drugs were withheld until the edema cleared; thyroid and vitamin B were given only after edema had disappeared; acacia, hypertonic solutions and aminophylline were not given. The diet protein was sometimes reduced from 65 Gm. to 40 Gm. daily until edema had cleared. The observations were made over a period of eight years in 626 separate periods of treatment of 402 cases. Patients with pronounced edema, 94 per cent with gross cardiopathy, tolerated the high fluid intake and the results were better than those formerly obtained with restriction of fluids. It is suggested that the regimen used is physiologically sound and clinically useful in the correction and prevention of the related phenomena of edema, oliguria or anuria and dehydration. Schemm believes that his observations call for a critical reexamination of the accepted clinical practice of fluid restriction in the presence of edema, and for revaluation of the accepted hypotheses regarding edema formation and congestive heart failure on which this practice is based.

Amphetamine Sulfate in Obesity.—Albrecht reports the results he obtained in treating 300 obese patients. The dosage varied from 10 mg. to 30 mg. daily in divided doses. Patients were started on 5 mg. of amphetamine sulfate twice daily, the drug to be given one-half to one hour before breakfast and the noon meal. Those who have a light breakfast and who eat their evening meal early were given the drug one hour before the noon meal and at 4 p. m. Nearly all who take the drug lose the uncontrollable desire to eat between meals. Patients can be put on a diet varying in calories from 450 to 1,500 with an excellent chance that they will stay on it after the drug is discontinued. This is an easy and rapid way to lose weight, and, under the guidance and supervision of a physician mindful of the contraindications to amphetamine therapy, relatively free from ill effects. The weight loss is not permanent; it is transient in the great majority of instances and returns when the drug is discontinued unless the patient remains on his special diet.

Spontaneous Pneumothorax.—Goldman and Roth report 3 cases of spontaneous pneumothorax observed at the Barnes Hospital, St. Louis. The first patient was a man aged 51 with congenital cystic disease of the lung. Removal of a large amount of air and the injection of the patient's own blood into the pleural cavity resulted in a rapid clinical cure. The second patient, a man aged 40, had complete atelectasis of the upper lobe of the left lung associated with a spontaneous pneumothorax. The pneumothorax had been present for eleven months. The collapsed lung rapidly reexpanded following bronchoscopy, and there was no evidence of disease in the lung following reexpansion. A careful survey of the literature shows only 1 previous report of atelectasis following idiopathic spontaneous pneumothorax. In the third case, one of spontaneous idiopathic hemopneumothorax, recovery was followed by a recurrence. This is the third reported case of recurrence of pneumothorax following spontaneous idiopathic hemopneumothorax. It has frequently been stated that adhesions follow hemopneumothorax and prevent recurrence.

Archives of Ophthalmology, Chicago

32:443-548 (Dec.) 1944

Ocular Symptoms of Psychogenic Origin. C. P. Oberndorf.—p. 443.
Gonioscopic Correlates of Responsiveness to Miotics. P. C. Kronfeld. —p. 447.
*Keratitis Neuroparalytica: Corneal Lesions Following Operations for Trigeminal Neuralgia. C. L. Pannabecker.—p. 456.
Blood Vessels of the Conjunctiva: Studies with High Speed Macrophotography. S. Gartner.—p. 464.
Binocular Papilledema in a Case of Torulosis Associated with Hodgkin's Disease. M. Cohen.—p. 477.
Krukenberg Spindle and Its Relation to Annular Pigmented Band on Periphery of the Lens. J. G. Bellows.—p. 480.
Pigmented Lines in Retroiridal Region of Anterior Capsule of Lens. J. G. Bellows.—p. 483.
Dacryocystitis: Transplantation Operation. H. Gifford, Jr.—p. 485.
Chronic Dacryocystitis: Treatment from the Rhinologist's Point of View. L. B. Spake.—p. 488.
Congenital Arterial Aneurysm at the Papilla. F. H. Theodore and W. H. Bonser.—p. 492.
Crystalline Lens in Diabetes Mellitus. J. G. Bellows.—p. 498.

Corneal Lesions Following Operations for Trigeminal Neuralgia.—According to Pannabecker members of the department of neurosurgery of the University Hospital at Ann Arbor, Mich., performed operations for trigeminal neuralgia in 878 cases during the period from 1927 to 1943. Corneal lesions followed in 18 per cent of these. It was found that operations on the lower branches of the trigeminal nerve which do not involve the first, or ophthalmic, branch do not cause damage to the cornea. Corneal anesthesia and lagophthalmos are the important factors in the production of corneal lesions. Combined corneal anesthesia and lagophthalmos give the greatest incidence of corneal lesions (65 per cent). With repeated operations a lesion occurring after the first operation may indicate that a lesion is likely to follow the second. But the incidence of lesions was not definitely greater with repeated operations than with single ones. Operations complicated by the presence of a neoplasm are more likely to be followed by paralysis of the seventh nerve and exposure keratitis. But the incidence of corneal lesions was not greater than with other complete rhizotomies. The prospect of neuroparalytic keratitis developing after complete rhizotomy on both sides is not greater than after a complete rhizotomy on one side and should not deter one from bilateral operation if severe pain is present. The patient with corneal anesthesia following operation for trigeminal neuralgia is most susceptible to development of neuroparalytic keratitis during the first few months immediately after operation. Treatment of this condition has varied somewhat, but the importance of closure of the lids has always been recognized. A mild antiseptic, such as an aqueous solution of metaphen 1:2,500 or of merthiolate 1:5,000 is prescribed. Isotonic solution of three chlorides is used frequently during the day if there is an indication of insufficient secretion of tears. Closure of the lids has been obtained by various means, such as padding the eye, closing with adhesive tape, use of the Frost suture and tarsorrhaphy. A Frost suture is the best procedure for temporary closing and is useful when the patient is uncooperative or comatose. A tarsorrhaphy is the best procedure for treating neuroparalytic keratitis or exposure keratitis—either a three band or an Elschnig lateral tarsorrhaphy, as indicated. The tarsorrhaphy should be left in place for six months. Cauterization of the punctum was employed in a limited number of cases. Cervical sympathectomy also has been advised. Prophylactic care should be used with any eye which is anesthetic. Temporal shields may be applied to the glasses, and isotonic solution of three chlorides should be used several times daily if the test for lacrimal secretion shows a deficiency of tears. Early tarsorrhaphy should be performed in doubtful or suspected cases. If the tarsorrhaphy is left in place for six months the patient will have been carried through the most critical period of this disease.

Canadian Medical Association Journal, Montreal

51:493-600 (Dec.) 1944

Bacteriologic and Clinical Observations on Local Treatment of Infections and Fresh Trauma with Penicillin Cream. D. Ackman and F. Smith. —p. 493.
Active Management (Nonoperative) of Craniocerebral Injuries (Disposition of 180 Canadians and Follow-Up of 132 Patients Returned to Active Service in Canadian Army). E. H. Botterell and K. E. Wilson.—p. 498.
Demerol in Surgery and Obstetrics. C. G. Hori and S. Gold.—p. 509.
Operative Treatment of Injuries to Semilunar Cartilages in Personnel of British Air Forces. D. M. Meekison.—p. 517.
Operation of Industrial Health Service. V. Ward.—p. 521.
Dangers of Incorrect Use of Iodine in Goiter Treatment. R. R. Fitzgerald.—p. 527.
Thyrocardiacs. A. L. Lockwood.—p. 532.
Sulfonamide Anuria. J. T. MacLean.—p. 536.
Practical Method for Supply of Fresh Milk to Isolated R. C. A. F. Stations. J. W. Tice, F. F. Tisdall and J. F. McCreary.—p. 541.
External Fixation in Fractures. J. W. Ross.—p. 543.
Alteration from Normal to Abnormal PR Interval with Change in Posture. G. W. Manning and C. B. Stewart.—p. 546.
Pneumonia Review of 425 Cases in Montreal, 1941-1943. E. S. Mills and D. McCallum.—p. 547.
*Anterior Poliomyelitis in Pregnancy. M. Blair and C. E. Robertson. —p. 552.
Infectious Mononucleosis. N. McGillivray.—p. 554.

Anterior Poliomyelitis in Pregnancy.—Blair and Robertson present their experience with pregnancy in the presence of maternal poliomyelitis at the Vancouver General Hospital. Six cases were observed over a period of twelve years, during which there were 25,427 deliveries. The first woman, eight months pregnant, died of respiratory paralysis. No Drinker apparatus was available at that time (1931). At necropsy the mother's spinal cord showed the typical changes of poliomyelitis. The fetus was well formed, and the spinal cord showed no pathologic changes. The second woman was admitted during the sixth month of pregnancy with paralysis of the lower limbs. Four weeks later a premature child died several hours after birth. Examination of the infant's spinal cord revealed no abnormalities. The mother's convalescence was uneventful. The third woman was in her sixth week of pregnancy and was admitted with neck stiffness, pain in the lumbar region and thighs and weakness of the extensor muscles of the thighs. She aborted spontaneously six days after admission. Her subsequent course was uneventful. The fourth patient had been pregnant four and one-half months when she entered the hospital complaining of nausea and vomiting, crampy pains in the calves and thighs, and soreness and stiffness of the neck and back. She was discharged after twenty days and later had a normal delivery. The fifth patient was admitted when six months pregnant with headache and pain in the lower legs and back. Both knee

jerks and the right ankle jerk were absent. There was a complete paralysis of the right lower limb and weakness of the left. She was discharged one month later with persisting paralysis of the flexors of the right hip and of the right tibialis anterior muscle. The patient was subsequently delivered, the course of labor being normal, as was the child. The sixth patient was three months pregnant when she developed symptoms of poliomyelitis and had to be placed in a respirator because of complete paralysis of the diaphragm and intercostal muscles. She gradually improved and at the time of her delivery was able to be outside the respirator for eleven of the twenty-four hours daily. She was taken to the labor room in the respirator but was removed from it for the actual delivery. The puerperium was normal. Paresis of the lower extremities and lower torso cleared early and her chief paresis was in the chest, arms and neck. She was conscious of labor pains and was able to help expel the baby over the perineum. The baby is well developed. The mother now walks about. The virus of poliomyelitis has never been demonstrated in the blood stream. If it is present it is never sufficient to invade the fetus. The safety of the child in utero, even in the presence of the most virulent attack compatible with life, is well demonstrated in this series.

Experimental Medicine and Surgery, Brooklyn

2:277-400 (Nov.) 1944

Transient Intraventricular Conduction Defect. B. Kisch and A. Grishman.—p. 277.
Effect of Penicillin and Choline on Appearance, Growth and Disappearance of Emge Sarcoma in Rats. H. H. Beard.—p. 286.
Experimental Use of Penicillin and Propamidine in Acute Purulent Arthritis. C. J. Frankel, R. W. Lee and R. B. Houlihan.—p. 290.
Functional Changes of Liver After Experimental Injury: Note on Dog's Tolerance for Glycine. E. C. Loomis and A. J. Quick.—p. 298.
Action of Carcinogenic Compounds and Related Substances on Enzymes. J. Feigenbaum.—p. 304.
Digestibility of Casein Derivatives by Digestive Tract. P. I. Fodor, S. Kuk-Meiri and A. Fodor.—p. 311.
Presystolic Murmur Without Auricular Systole: Clue to Genesis of Auricular Sounds. F. M. Groedel and B. Kisch.—p. 319.
Influence of Chest Wall on Heart Sounds. F. M. Groedel and M. Miller. —p. 328.
Studies on Insensible Loss of Water. E. R. Zak and G. C. Leiner. —p. 339.
Physiologic and Pathologic Asynchronism of Function of Heart Chambers. F. M. Groedel.—p. 352.

Journal of Immunology, Baltimore

49:321-391 (Dec.) 1944

Serologic Types of Shigella Paradysenteriae (Flexner). A. J. Weil, J. Black and K. Farsetta.—p. 321.
Failure to Sensitize Guinea Pigs Passively with Equine Antisera That Fix Guinea Pig Complement. Edna M. Follensby and S. B. Hooker. —p. 353.
Studies on Technic of Collodion Agglutination: Influence of Certain Qualities of Collodion Particles and of Proportions of Antigen and Collodion on Sensitivity and Specificity of Reaction. P. A. Cavelti. —p. 365.
Neutralization Tests with Certain Neurotropic Viruses: Comparison of Sensitivity of Extraneural and Intracerebral Routes of Inoculation for Detection of Antibodies. E. H. Lennette and H. Koprowski.—p. 375.

Journal of Nat. Cancer Inst., Washington, D. C.

5:151-232 (Dec.) 1944

Growth and Pathology of Melanoma S91 in Mice of Strains dba, A and C. G. H. Algire.—p. 151.
Role of Heredity in Tumor Development. W. E. Heston.—p. 161.
Attempts to Produce Anaphylaxis in Guinea Pigs with a Polysaccharide from Serratia Marcescens (Bacillus Prodigiosus). F. E. Franke. —p. 173.
Effects of Sublethal Doses of Polysaccharide from Serratia Marcescens (Bacillus Prodigiosus) on Electrocardiogram, Blood Ascorbic Acid and Nonprotein Nitrogen of Dog. F. E. Franke and D. Richert.—p. 179.
Action of Toxic Doses of Polysaccharide from Serratia Marcescens (Bacillus Prodigiosus) on Dog and Guinea Pig. F. E. Franke.—p. 185.
Chemical Treatment of Tumors: X. Reactions of 4 Patients with Advanced Malignant Tumors to Injection of Polysaccharide from Serratia Marcescens Culture Filtrate. A. M. Brues and M. J. Shear. —p. 195.
Degradation of Cystine Peptides by Tissues: I. Exocystine Desulfurase and Dehydropeptidase in Rat Liver Extracts. J. P. Greenstein and Florence M. Leuthardt.—p. 209.
Degradation of Cystine Peptides by Tissues: II. Distribution of Exocystine Desulfurase and Dehydropeptidase in Tissue Extracts of Various Species. Jesse P. Greenstein and Florence M. Leuthardt.—p. 223.
Gastric Function of Dogs After Stimulation with Acetyl-B-Methylcholine Chloride and Histamine Diphosphate. Helen Dyer and Margaret G. Kelly.—p. 227.

Journal of Nervous and Mental Disease, New York

100:555-672 (Dec.) 1944

Psychiatric Sequelae of Post-Measles Encephalitis (Study of 21 Cases). E. C. Smith and C. E. Trapp.—p. 555.
Prognostic Value of Clinical Findings in Cases Treated with Electric Shock. L. Gold and C. J. Chiarello.—p. 577.
Panoramic Position of Psychiatry (Psychosomatic Medicine, Psychotherapy, Hypnotism, Shock Therapy). A. N. Foxe.—p. 584.
Evaluation of Prognostic Criteria in Schizophrenia. O. Kant.—p. 598.
Dilemma of Etiologic Concepts of Mental and Organic Disease. J. Perlson.—p. 606.

Journal of Pediatrics, St. Louis

25:461-646 (Dec.) 1944

Metabolic Basis for Individualized Feeding of Infants, Premature and Full Term. H. H. Gordon and S. Z. Levine.—p. 464.
Congenital Malformations Induced by Maternal Nutritional Deficiency. J. Warkany.—p. 476.
Age as Factor in Streptococcosis. G. F. Powers and P. L. Boisvert. —p. 481.
*Penicillin: Its Use in Pediatrics. W. E. Herrell and L. J. Kennedy. —p. 505.
Treatment of Type B. Hemophilus Influenzae Meningitis. Hattie E. Alexander.—p. 517.
Diagnosis of Rh Incompatibility, Especially by Microscopic Appearances: Its Relation to Syndrome Formerly Diagnosed as Erythroblastosis. Madge Thurlow Macklin.—p. 533.
Bacterial Enteritis. G. Varela.—p. 555.
Arthropod Borne Diseases. E. C. Faust.—p. 563.
Whooping Cough. N. Silverthorne.—p. 584.
Multiple Neuropathy, Grade 3. J. A. Toomey and J. Messina.—p. 590.

Penicillin in Pediatrics.—Penicillin has been used in the pediatric service of the Mayo Clinic in the treatment of 54 patients with various types of bacterial infection. For the local treatment of most bacterial infections in infants a total daily dose of 20,000 to 40,000 units of either the sodium or the calcium salt appears to be adequate. For larger children a total daily dose of 60,000 to 80,000 units is as a rule enough with the possible exception of cases of overwhelming sepsis, in which it may be desirable to use as much as 100,000 to 150,000 units. For the local treatment of wounds involving soft tissues as well as bone, saline solutions containing 250 to 500 Oxford units of penicillin per cubic centimeter are suitable. Penicillin may be administered locally in the form of the dry substance alone or in combination with sulfanilamide. These sulfanilamide-penicillin powders usually contain 5,000 units of penicillin per gram of sulfanilamide. Penicillin may also be administered locally as a cream containing 250 units of penicillin per gram. For local therapy the calcium salt of penicillin is preferred to the sodium salt. For systemic administration to infants the intermittent intramuscular method is the best. From 3,000 to 5,000 units should be administered in 1 or 2 cc. of isotonic solution of sodium chloride every three hours, day and night. In overwhelming sepsis as much as 10,000 units may be given by the intramuscular method every three hours. In larger children penicillin can be administered by the continuous intravenous drip. In certain instances, such as extensive burns, in which suitable sites for intramuscular injection are not available, it may be desirable to resort to the infusion of penicillin by way of the bone marrow. The sternum or clavicle can be used satisfactorily. Forty-five of the 54 cases responded favorably. Penicillin was effective in bacteremia, severe cellulitis, acute osteomyelitis, meningitis, pulmonary suppurative disease, certain pyogenic skin infections, otitis media, actinomycosis and a group of miscellaneous infections including septic arthritis and ocular infections. Penicillin is of little or no value in gram negative bacillary infections, including undulant fever, tularemia, influenza or infections due to the colon-typhoid-dysentery group of organisms or to Friedländer's bacillus. Infections of the urinary tract due to the gram negative organisms do not respond to penicillin. It is of no value in tuberculosis, acute rheumatic fever, rheumatoid arthritis, ulcerative colitis, malaria or blastomycosis. It is useless in leukemia as well as in certain skin diseases including lupus erythematosus. The advantage of penicillin over sulfonamides resides not only in its greater antibacterial powers but also in the low incidence of toxic manifestations.

Journal of Pharmacology & Exper. Therap., Baltimore

82:203-302 (Nov.) 1944

Value of Guinea Pig Corneal Reflex for Tests of Surface Anesthesia. M. R. A. Chance and H. Lobstein.—p. 203.
Evaluation of Assay of Vitamin P by Means of Effect of Low Pressure on Mice. A. C. Kibrick and A. E. Goldfarb.—p. 211.
Effect of Administration of Sodium Bromide to Pregnant Rats on Learning Ability of Offspring: II. Maze Test. B. K. Harned, H. C. Hamilton and V. V. Cole.—p. 215.
Quantitative Study of Effects of Ouabain on Electrocardiogram. L. Apter, R. Ashman and E. Hull.—p. 237.
Renal Elimination of Sulfamerazine, Sulfamethazine, Sulfadiazine and Sulfathiazole by Dog. K. H. Beyer, L. Peters, Elizabeth A. Patch and H. F. Russo.—p. 239.
*Neutralization of Gastric Acidity with Basic Aluminum Aminoacetate. J. C. Krantz Jr., Dorothy V. Kibler and F. K. Bell.—p. 247.
Protection Against Lethal Doses of Pentavalent Arsenical and Antimonial Compounds in Rats by p-Aminobenzoic Acid, a Histologic Study. P. N. Harris.—p. 254.
Effect of Acid and Alkali on Absorption and Metabolism of Quinine. J. C. Andrews and W. E. Cornatzer.—p. 261.
Studies on Synthetic Curare-like Compounds: III. Toxicity and Curarizing Action of Some New Quinine Derivatives. H. F. Chase, A. J. Lehman and Eleanor E. Rickards.—p. 266.
Pharmacologic Studies of New Vasoconstrictor: 2-Naphthyl-(1')-Methyl-Imidazoline Hydrochloride (Privine or Naphthazoline): II. Vascular and Respiratory Reactions in Anesthetized Dog. B. N. Craver, H. F. Chase and F. F. Yonkman.—p. 275.
Anesthesia: XVI. Determination of Isopropenyl Vinyl Oxide in Blood of Anesthetized Animals. W. E. Evans Jr., C. J. Carr, Virginia M. Waters and J. C. Krantz Jr.—p. 288.
New Aerobic Metabolite Whose Production by Brain is Inhibited by Apomorphine, Emetine, Ergotamine, Epinephrine and Menadione. H. I. Kohn and Margaret Liversedge.—p. 292.
Dinitrophenol Cataract in Chick: Effect of Age. B. H. Robbins.—p. 301.

Neutralization of Gastric Acidity.—Krantz and his associates observed the lag in acid absorbing and neutralizing capacities of various samples of aluminum hydroxide gel. A new compound, the basic aluminum salt of aminoacetic acid, was found to have the capacity to buffer and neutralize hydrochloric acid. Its prompt and prolonged buffering of acid suggested its use in the treatment of hyperacidity and peptic ulcer. On the basis of the aluminum content, basic aluminum aminoacetate is 42 per cent more efficient in acid consuming power than dried aluminum hydroxide gel. Feeding studies on rats did not result in abnormalities. Basic aluminum aminoacetate was administered to 20 persons in doses of 2 to 4 Gm. in powder form suspended in water. It was tolerated without symptoms. Two patients with active peptic ulcer were treated with the salt as the sole antacid. Healing was observed by the gastroscope and the patients became asymptomatic. In 2 cases of latent peptic ulcer with postprandial distention and hyperacidity prompt and prolonged relief followed ingestion of 0.5 Gm. compressed tablets of the salt. Extensive clinical investigations with the compound are in progress.

Minnesota Medicine, St. Paul

27:991-1062 (Dec.) 1944

Significance of Rheumatic Fever to Community. H. McCulloch.—p. 991.
Consideration of Physiologic Action of Thiouracil and Other Goitrogens. G. M. Higgins.—p. 997.
Thiouracil: Therapy in Hyperthyroidism. G. T. Evans and E. B. Flink.—p. 1002.

New England Journal of Medicine, Boston

231:781-816 (Dec. 14) 1944

Plea for Thought Taking in Medical Treatment of Cholecystitis. W. C. Alvarez.—p. 781.
Surgical Aspects of Gallstones. H. M. Clute and F. R. Kenney.—p. 783.
Radiologic Aspects of Gallbladder Disease. M. C. Sosman.—p. 786.
Endocrine Aspects of Cancer. I. T. Nathanson.—p. 795.

231:817-864 (Dec. 21) 1944

*Use of Sulfadiazine as Prophylactic Against Respiratory Disease. R. C. Hodges.—p. 817.
Prevention of Pulmonary Embolism. C. A. Robinson.—p. 821.
Frank Burr Mallory: A Doctor of Physicians. W. Freeman.—p. 824.
Sulfonamide Therapy in Otolaryngology. R. L. Goodale.—p. 829.

Sulfadiazine as Prophylactic Against Respiratory Disease.—Hodges states that hospital admissions for streptococcic and pneumococcic infections from an Army Air Force technical school rose alarmingly during January 1944. The experience of the previous year suggested that serious epidemics were beginning. Administration of sulfadiazine was made throughout February and March. The results appeared to be beneficial. The most striking effect was on beta-hemolytic streptococcus infection. It appeared that streptococcic sore throat and scarlet fever could be reduced almost to zero. There was a less evident but still significant effect on pneumococcic infection. Sixteen weeks after the onset of the epidemic of streptococcic infection the incidence of acute rheumatic fever was well below the accepted rate. Ordinary respiratory disease also showed a response to the drug. This is thought to be due to the fact that streptococci and pneumococci give a clinical picture indistinguishable from that of the common cold, although this concept remains to be proved. A variety of dosages was tried. It is believed that the optimal dosage for a given group should be worked out individually. No serious untoward reactions occurred.

Radiology, Syracuse, N. Y.

43:531-637 (Dec.) 1944

X-Ray Evidence of Old Forgotten or Previously Undiagnosed Fractures. J. E. Habbe and H. H. Wright.—p. 531.
Induction Film as an Aid in Appraising Subsequent Pulmonary Lesions. A. N. Alpern and J. E. Benjamin.—p. 548.
Roentgenologic Aspects of Retroperitoneal Perforations of Duodenum. E. A. Jacobs, G. J. Culver and E. C. Koenig.—p. 563.
Dosage Table for Linear Radium Sources. Edith H. Quimby.—p. 572.
Priodax: A Contrast Medium for Cholecystography: Analysis of 163 Cases, Outlining Various Reactions in Three Technics and Operative Findings in 22 Cases. W. W. Vaughan and M. Eichwald.—p. 578.

War Medicine, Chicago

6:353-438 (Dec.) 1944

Experiences with Anesthesia in Combat Areas. I. R. Hayman.—p. 353.
Validity of Psychiatric Criteria for Rejection for Service with the Armed Forces: Study of Cases of 696 Registrants with Psychiatric Diagnoses from New York City Selective Service Area. S. J. Kopetzky.—p. 357.
*Acute High Altitude Anoxia: Gross and Histologic Observations in 27 Cases. R. A. Kritzler.—p. 369.
Chemotherapy in Intracranial Infections: V. Treatment of Staphylococcic and Pneumococcic Meningitis with Sulfathiazole and Sulfadiazine. W. F. Meacham, E. Smith and C. Pilcher.—p. 378.
Marihuana Addict in Army. E. Marcovitz and H. J. Myers.—p. 382.
Altered Taste in Dengue. S. R. Elek.—p. 392.
Protective Effects of Preoxygenation on Abdominal Gas Pain: Results of Study of Preflight Breathing of Oxygen on Pain Resulting from Decompression to 38,000 Feet. F. M. Henry, J. H. Lawrence, E. V. Bridge and O. L. Williams.—p. 395.

High Altitude Anoxia.—Fatalities in air crews due to deprivation of oxygen during bombing operations at high altitude afforded an opportunity to study the gross and microscopic anatomy of acute anoxia in man as it occurs at low atmospheric pressure. Twenty-seven necropsies were performed during 1943 in one hospital on members of high altitude bomber crews in which death had been attributed to anoxia by the Air Force medical officers who investigated the cases. Widespread, severe capillary congestion was found. This was conspicuous and most constant in the pulmonary, renal, intestinal and cerebral capillaries. The skeletal muscle did not show this congestion. In a high proportion of cases the systemic venous and the portal circulations showed gross and microscopic congestion, with dilatation of the right ventricle. There was wide individual variation in the incidence, location and amount of edema and hemorrhage. An exception to this was the consistent occurrence of hemorrhage in the thymus and in the middle ear. Swelling of endothelial cells of capillaries of the renal medulla was observed. The presence of fat free and glycogen free vacuoles previously described in the myocardium and liver and less frequently in cells of other organs was confirmed. These vacuoles occurred with equal frequency in cases of anemic anoxia (acute carbon monoxide poisoning) but were rarely found in the tissues in nonanoxic control cases.

West Virginia Medical Journal, Charleston

40:373-404 (Dec.) 1944

Tuberculosis in West Virginia Industries. J. T. Duncan and C. S. McKinley.—p. 373.
Newer Methods of Communicable Disease Control. L. F. Badger.—p. 378.
Observations on Improved Disease Control Methods Among Troops. J. W. R. Norton.—p. 382.
Hyperthyroidism and Thiouracil. Case. F. R. Whittlesey.—p. 385.
Primary Carcinoma of Both Breasts: Case. R. K. Buford and M. A. Iatesta.—p. 386.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Tuberculosis, London

38:105-140 (Oct.) 1944

"What Is the Right Time, Please?" Surgeon's Answer. J. E. H. Roberts. —p. 105.
*Carbon Dioxide by Inhalation in Management of Cough. A. L. Banyai and A. V. Cadden.—p. 111.
Mass Miniature Radiography in Royal Air Force. R. R. Trail and others.—p. 116.

Inhalation of Carbon Dioxide for Cough.—Banyai and Cadden have used carbon dioxide by inhalation as an expectorant in pulmonary tuberculosis for the past thirteen years. It changes an excessive yet unproductive cough into a useful cough and thereby often helps to eliminate the dangers inherent in an accumulation and retention of inflammatory products. Carbon dioxide liquefies the mucopurulent exudate in the bronchi and reduces its viscosity; the sputum is loosened up and consequently is expectorated without strain or effort. Adequate evacuation of the bronchi ensures comparatively long periods of rest free from annoying cough. The apparatus used by the authors consists of a tank containing a mixture of 10 per cent carbon dioxide and 90 per cent oxygen. An oxymeter regulates the flow of gas per minute. In some patients it was found expedient to give the inhalation through a glass tube instead of the mask. The open method is recommended for patients who are debilitated or who show some side effects when the closed inhaler is used. The meter is set for 4 to 5 liters per minute for closed inhalations and for 5 to 7 liters per minute for the open method. The treatments vary in length from five to fifteen minutes, and the inhalations are administered once, twice or three times a day. It is necessary to observe the patient closely during the first treatment. If it is noted that the respirations become too strenuous, the inhalations should be given with brief (one minute) interruptions. In the beginning the treatments are given daily; subsequently the frequency of inhalations can be reduced. Almost all patients tolerate carbon dioxide inhalations well, provided the amount of the inhaled gas and the timing of inhalations are individually adapted to the patient's requirements. In some patients they noted transient minor side effects, such as hot sensations, palpitation, weakness, frontal headache and slight dizziness. None of these symptoms interfered with the treatment when proper adjustments were made in the method of administration. The liquefying effect of carbon dioxide on mucopus in the bronchial tract is greater than that of the commonly used expectorants. Carbon dioxide by inhalation occupies a unique place among expectorants in that, besides its liquefying action, it is capable of stimulating the respiratory center. Stimulation of the respiratory center causes increased respiratory expansions of the thorax, a consequent stretching and dilatation of the bronchi and an increase in the bronchial peristalsis. These factors contribute substantially to the effective mechanical elimination of inflammatory products from the respiratory tract.

British Medical Journal, London

2:683-714 (Nov. 25) 1944

*General Anesthesia in Shock. A. C. Crooke, C. J. O. R. Morris and R. G. Bowler.—p. 683.
*Use of Penicillin Pastilles in Oral Infections: Preliminary Report. A. B. MacGregor and D. A. Long.—p. 686.
*Analysis of 259 of Recent Flying Bomb Casualties. R. C. Bell.—p. 689.
Massive Surgical Emphysema During Course of General Anesthesia. N. R. Barrett and D. Thomas.—p. 692.
Unusual Case of Generalized Tuberculosis. W. H. Mylechreest and I. M. Scott.—p. 693.

General Anesthesia in Shock.—Crooke and his associates show that operations on seriously shocked patients are associated with a notoriously high mortality. This may be due to further loss of blood entailed during the operation, to the stimulus of the operative manipulations or to the anesthetic. It has become apparent that the most important single factor has been the anesthetic, and an examination has therefore been made of the effect of different anesthetics on the cardiovascular systems of 26 patients with normal plasma volumes, of whom 19 underwent various major operations—the majority a partial gastrectomy. In all cases the pulse and respiratory rates and the blood pressure were recorded at about three minute intervals. Determinations of plasma volume were made and the dye concentration curves followed at about thirty minute intervals until the end of the operation. The hemoglobin was also determined at the same intervals. Electrocardiographic records were made of 9 patients who underwent major operations. The anesthetics used were nitrous oxide, oxygen and ether, cyclopropane and oxygen, sodium pentothal and spinal analgesics. No significant changes were found, although great alterations in blood pressure occurred. Serial electrocardiograms in 9 patients showed a constant change even though a considerable alteration in blood pressure had taken place. It is concluded that anesthetics affect blood pressure mainly through the vasomotor system. Cyclopropane and oxygen tended to raise the blood pressure; nitrous oxide, oxygen and ether had variable effects on it; sodium pentothal and spinal analgesics depressed it. In a patient whose plasma volume was reduced by trauma there was a greater tendency for these anesthetics to depress blood pressure. Cyclopropane and oxygen was the best and nitrous oxide with adequate oxygen and a minimal amount of ether was the next best anesthetic for these cases.

Penicillin Pastilles in Oral Infections.—MacGregor and Long selected gelatin as a medium for penicillin pastilles. Care was taken that the penicillin was not subjected to excessive heat; it was added to the gelatin base at 42 C. and stirred in just before the latter was about to set. Pastilles were cut to a standard size of approximately ⅜ inch square and ⅛ inch thick to facilitate insertion and retention in the buccal sulcus. It was shown in experiments that the penicillin remained active in the gelatin base. The standard dose adopted was 500 units of penicillin in each pastille. Each patient was instructed to place a pastille in the buccal sulcus, to leave it there until it had dissolved without chewing or sucking and then to replace it with another. The time taken for the pastille to dissolve varied in different patients and in general tended to be shorter in the earlier and more acute stages of the infection owing to the greater degree of salivation. The average was about three quarters of an hour. The penicillin pastilles were used on 25 patients with acute ulcerative gingivostomatitis (Vincent's type). It was found that this condition can be treated more simply and more quickly with penicillin pastilles than by any other method. The loss of tissue caused by the more usual treatments with caustics and escharotics can be avoided. The penicillin pastilles were used also for 17 patients with acute hemolytic streptococcic tonsillitis, including 4 with scarlet fever. The patients seemed to respond clinically to treatment with pastilles. The effect on the throat flora appeared to be rapid. The early disappearance or reduction in numbers of hemolytic streptococci in the throat suggests that the risk of droplet infection is greatly reduced. The treatment of throat carriers of hemolytic streptococci proved disappointing. It is of interest that they became negative while undergoing treatment. It appeared that surgical conditions of the mouth and throat could be kept free from pathogenic organisms during administration of the pastilles, with gratifying symptomatic relief. On bacteriologic grounds faucial diphtheria should be an indication for treatment with penicillin pastilles.

Flying Bomb Casualties.—Bell describes injuries caused by the flying bomb raids as seen in a small hospital of the Emergency Medical Service. His hospital dealt with 222 outpatients and 256 inpatients, with 18 deaths. Flying glass was the most frequent cause of injury, totaling over 100 casualties. Most of the injuries were above the nipple line, chiefly of the face and neck; a large proportion were received when looking out of windows. There were 5 cases of perforating wounds of both eyes and 10 perforating wounds of one eye. The penetrating power of flying glass is low. Usually it lies just under the skin in the fat, but when present in hundreds of pieces it presents a problem which has not yet acquired a satisfactory solution. The rarity of penetrating wounds is due to the shape of the fragments, which tend to be small flat pieces of metal. Occasionally the bomb fragments are large tangled masses of crumpled sheeting weighing a pound or more, and these may cause severe injuries. In the beginning injuries from masonry were uncommon. Later they became more frequent as adequate

cover was taken, and instead of being killed the victims were buried with various degrees of trauma. There was not a single case of crush syndrome with edema of the injured part, anuria and uremia. This is probably due to the increased speed of the rescue service and possibly to a lessening in the enthusiasm for intravenous plasma therapy. The injuries tended to be severe, and there was a proportionately high death rate (9 out of 52). It was difficult to estimate the number of patients whose lungs were affected by blast and to assess the relative damage caused by blast in contradistinction to other agents. Three patients had severe pain in the chest, breathlessness and traces of blood in the sputum. One of these died. At necropsy he was discovered to have gross contusion of the left side of the brain and of the left lung, a small split in the capsule of the spleen and a hematoma over the left femur. Microscopy showed blood cells among the brain tissues and blood cells in most of the alveoli of the left lung. Many of the alveolar walls were torn. It is difficult to decide on the exact part played by blast in eye injuries. There were 4 hyphemias which were not explicable except as the result of blast. In injuries of the brain it was also difficult to decide whether blast had been the sole agent. Corneal abrasions due to dust were common. The respiratory system also suffered from the effects of dust. At operation the anesthetist remarked time and again on the dirt in the pharynx and trachea. An air raid warden reported that several of the dead had been suffocated by dust, the mouth, nose and throat being completely blocked, while no other injuries were visible. Psychologic shock was the term coined to cover hysteria, fright and mental upset requiring only rest and reassurance.

Lancet, London

2:647-678 (Nov. 18) 1944

Lung Abscess: Pathology and Diagnosis of Certain Types. N. R. Barrett.—p. 647.
Direct Laryngoscopy and Tracheal Intubation. F. B. Bannister and R. G. Macbeth.—p. 651.
Paroxysmal and Postural Headaches From Intraventricular Cysts and Tumors. W. Harris.—p. 654.
Alloxan Diabetes in Monkeys. S. Bannerjee.—p. 658.
*Fatal Coronary Sclerosis in Boy of Ten Years. E. Jokl and J. Greenstein.—p. 659.

Fatal Coronary Sclerosis in Boy of Ten.—Jokl and Greenstein report that a boy aged 10 collapsed and died five minutes after a boxing match lasting three rounds. He had received a number of blows against the chest and abdomen but was not knocked down, nor did he seem to be unduly distressed at any time during the fight. At necropsy the left descending branch of the coronary artery was blocked for a distance of about an inch. Above and below the occlusion were slight atheromatous changes in the intima.

Quarterly Journal of Medicine, Oxford

13:37-105 (April-July) 1944

*"Fibrositis" of Back. W. S. C. Copeman and W. L. Ackerman.—p. 37.
*Proteolyzed Liver in Treatment of Refractory Anemias. L. J. Davis and L. S. P. Davidson.—p. 53.
Critical Review of Pernicious Anemia of Pregnancy. Sheila T. E. Callender.—p. 75.

Fibrositis of Back.—Copeman and Ackerman say that the frequency of fibrositis of the back seen among otherwise healthy young men in the army stimulated their interest in this condition. As a first step, exact measurements were taken of the site of the painful focus in a large number of sufferers and a "pain chart" was plotted. The back of every patient who died in the hospital from any cause was then systematically examined, with special reference to these areas. As a result of this and of subsequent clinical observations and biopsies, conclusions have been arrived at which seem to explain certain cases of "fibrositis." The authors say that their previous observation that the painful points may arise during any pyrexial illness or as the result of trauma was confirmed; also that the subjective pain disappears but that the point often remains and can be detected by tenderness on palpation. It can be reactivated subsequently and may become the seat of chronic pain. The back was carefully dissected in 14 bodies with particular reference to the chief sites of pain. It was found that a basic fat pattern was constantly present even in the most cachectic subjects in whom all other fat was absent. This fat pattern was observed to correspond in shape and situation with the pain pattern. No lesions suggestive of inflammatory reaction were found in any deep fibrous tissue, but abnormalities affecting the lobules of the fat pattern were found on several occasions. The abnormality which seemed most likely to have clinical significance was the herniation of fat lobules through the walls of their investing fibrous tissue. These fat hernias have been classified into three types: the nonpedunculated, the pedunculated and the foraminal. In the nonpedunculated type, fat which lies under a fascial covering, as for instance in the angle of the deep fascia where it splits to invest the sacrospinalis muscle, or along the crest of the ilium, is always under tension and so will bulge into any potential hernial space that may be present either as the result of congenital weakness or as the result of trauma. The pedunculated type of hernia has been found and removed in several instances. In these cases the onset of the pain was produced by a sudden strain several years previously. It is thought therefore that it is probably a late result of strangulation in a hernia originally of the nonpedunculated type. The foraminal type of hernia was found only along the edges of the sacrospinalis muscles. These areas were exposed in the cadavers, and it was found that the nerves passed out in company with a small artery and vein through a foramen in the deep fascia of the muscle. Overhanging this was a narrow lateral fold of the fascia so arranged as to occlude the foramen on flexion of the back. In several cases it was seen that this mechanism had apparently proved ineffective and a small tuft of fat lobules had also herniated through the foramen. The authors suggest that the anatomic conditions which they have described represent a comparatively advanced stage in the process and that to explain the minor and less localized degrees of fibrositis it is not necessary to postulate actual herniation of fat tissue. They describe biopsies on 10 selected patients with fibrositis. Their observations at biopsy led them to evolve a technic of treatment which they call "teasing" the nodule. This consists in anesthetizing a small area of skin over the site of the trigger point, which has previously been ringed with a skin pencil. It is then transfixed with a stout rigid needle, and after injection of 10 to 20 cc. of 1 per cent procaine solution under the greatest pressure possible the point of the needle is swept round deeply in such a way as to undercut the nodule.

Proteolyzed Liver in Refractory Anemias.—Davis and Davidson administered orally proteolyzed liver, a papain digest of whole liver, to 13 patients with severe anemia refractory to treatment with potent liver extracts administered parenterally. In 5 patients the morphology of the peripheral blood and sternal marrow was respectively macrocytic and megaloblastic. A megaloblastic marrow smear is identical in appearance with that seen in addisonian pernicious anemia in relapse. In such smears a high proportion of the erythroblasts are large cells with abundant dark blue cytoplasm and large nuclei displaying a finely reticulated structure in which nucleolar remnants may or may not be seen. Many of the more mature red cell precursors which show varying degrees of hemoglobination are distinguished from normoblasts by their relatively greater size and particularly by the loosely woven character of the nuclear chromatin. The 5 patients with refractory anemias with megaloblastic sternal marrows were an elderly woman, a child, a middle aged man, a young man and a young woman in the puerperium. In all these 5 patients administration of proteolyzed liver resulted in a prompt and vigorous hemopoietic response and the rapid restoration of the patient to normal health. In 3 other patients the anemia was also macrocytic, but the sternal marrow films showed dimorphic erythropoiesis. The authors consider the term dimorphic a convenient provisional designation for sternal marrow films showing erythropoiesis which is predominantly normoblastic but partially megaloblastic. In these 3 patients treatment with proteolyzed liver was followed by only partial blood regeneration with the survival of the patients in moderate health. The remaining 5 of the 13 patients had anemia of the aplastic type with hypocellular normoblastic sternal marrow, and they completely failed to respond to proteolyzed liver or to any other form of treatment. It is suggested that proteolyzed liver contains in a readily assimilable form some hemopoietic maturation factor additional to the antianemic factor present in fractionated liver extracts.

Chinese Medical Journal, Washington, D. C.

62:1-110 (Jan.-March) 1944

Calcium and Phosphorus Metabolism in Osteomalacia: Availability of Inorganic, Phytin and Dietary Phosphorus and Effect of Vitamin. D. K. Wang, S. H. Liu, H. I. Chu, T. F. Yu, H. C. Chao and H. C. Hsu.—p. 1.
Solustibosan in Treatment of Kala-Azar. H. L. Chung, C. W. Wang and C. U. Lee.—p. 17.
New Sodium Salt of Mannite Antimonic Acid in Treatment of Kala-Azar in Chinese Hamsters. H. L. Chung and H. K. Chow.—p. 26.
Prevention and Treatment of Common Nutritional Deficiency Diseases. H. C. Hou.—p. 32.
Investigation of Infant Mortality and Its Cause in Chengtu. M. Y. Cheng.—p. 47.
*Use of Honey in Treatment of Chilblain, Nonspecific Ulcers and Small Wounds: Preliminary Report. K. L. Yang.—p. 55.
Roentgenologic Anatomy of Position of Coils of Normal Small Intestine. F. Y. Khoo, K. S. Liu and K. H. Ch'en.—p. 61.

Honey in Treatment of Chilblain, Ulcers and Wounds.—Yang says that in the dermatologic clinic of the National Medical College at Shanghai cod liver oil ointment has been used in the treatment of chronic leg ulcers and small wounds and has been found to be very effective. This success is attributed to its rich vitamin A content, which has the property of stimulating epithelization and granulation tissue formation. After the medical college was moved to Kunming in 1939 the difficulty in obtaining cod liver oil prohibited its further use. It occurred to the author that honey might be employed as a substitute, the rationale of such treatment being that, owing to its high sugar content, it is bacteriostatic; while, owing to its yellow pigment, it might be rich in vitamin A. A honey ointment was made by the addition of 20 per cent of petrolatum. The ointment was first used with encouraging results in leg ulcer. Later when the medical college was moved from Kunming to Chungking it was decided to resume the honey treatment, but, since petrolatum was not obtainable, lard was used instead. The ointment, composed of 80 per cent honey and 20 per cent lard, was used in 50 cases of chilblain, chilblain ulcers, ordinary ulcers and small wounds. Its success in hastening the subsidence of passive hyperemia and edematous swelling, and in stimulating epithelization and granulation tissue formation, was great. Its application is simple and convenient, and its sources of supply are plentiful, thus being especially useful under present wartime conditions.

Wiener klinische Wochenschrift, Vienna

56:21-40 (Jan. 15) 1943

*Value of Liver Puncture in Diagnosis of Various Diseases of Liver. I. Hatieganu, T. Spärchez, P. Radu and I. Macavei.—p. 21.
Carcinoma and Sexuality. H. Truttwin.—p. 28.
Sedimentation Rate of Red Blood Corpuscles in Blood of Right and Left Side of Heart. M. Bénard.—p. 31.

Liver Puncture in Diagnosis of Liver Diseases.—Hatieganu and his associates report 45 cases in which a 2 cc. glass syringe and a long thin needle were employed in puncture of the liver. Puncture should be performed in the morning on an empty stomach half an hour after the administration of 15 drops of pantopon (a mixture of the hydrochlorides of opium alkaloids, containing 50 per cent of anhydrous morphine hydrochloride). By applying slight suction a punctate may be obtained rich in liver tissue with only a small amount of blood. The term hepatogram is applied to the cytologic preparation of the punctate on the microscopic slide. Liver puncture was performed in 11 cases of tumor of the liver, proving its value as biopsy. A definite early diagnosis in the initial stage of carcinoma was made from the hepatogram, which is characterized by lack of uniformity of the cells associated with an abnormal increase and irregular arrangement. Liver puncture is an aid to differential diagnosis of liver carcinoma from liver sarcoma, particularly from that of melanosarcoma. The deep dark pigment in the form of round, egg shaped granules fills almost the entire protoplasm of the cell and is localized about the nucleus. Cellular alterations may likewise be demonstrated on the hepatogram of grave cases of parenchymatitis of the liver, particularly in icterus of cholangitic type. Puncture may be of practical importance in cases of pigmentary cirrhosis in which medium sized, single or accumulations of brown granules may be found within or outside the protoplasm even in atypical cases which do not present bronzed skin. Immature blood elements may be demonstrated in the hepatogram in leukemia; the premyelocytes and myelocytes may be predominant; there may be a few myeloblasts, and basophil erythroblasts may likewise be found. The microscopic picture of a hepatogram in acute leukemia resembles that of the myelogram, so that liver puncture may be dispensed with in these cases, although it may have its value in aleukemic and erythroblastic leukemia. In pernicious anemia the megaloplastic function of the liver may be demonstrated in the hepatogram. Liver puncture may reveal the causative agent in cases with a slow septic course and may clarify the bacteriologic diagnosis of the condition.

Khirurgiya, Moscow

4:3-18, 1944. **Partial Index**

Volatile Oils in the Treatment of Infected Wounds: Part I. O. T. Shishkina.—p. 3.
Volatile Oils in the Treatment of Infected Wounds: Part II. P. V. Lebedinskiy.—p. 7.
*Cervical Vagus-Sympathetic Block in the Treatment of Shock. S. P. Skvortsov.—p. 11.
Local Anesthetic Block for Penetrating Wounds of Thorax. A. G. Karavanov.—p. 15.
*Vagus-Sympathetic Block. A. V. Vishnevskiy.—p. 16.

Vagus-Sympathetic Block in Shock.—Skvortsov applied the method of procaine hydrochloride infiltration anesthesia of the vagus nerve and the sympathetic nerve in the neck in a variety of war casualties such as open pneumothorax, abdominal operations and lesions of extremities when the men were brought in in a state of shock. In cases of open pneumothorax the method resulted in raising the blood pressure in from five to ten minutes 13 to 15 mm. of mercury in 88 per cent of the cases. Pain and dyspnea disappeared in about 91 per cent, the cough reflex disappeared and manifestations of shock gradually disappeared in the course of an hour and a half to two hours. The fact that the vagus-sympathetic block raises the blood pressure within three to five minutes of its application suggests that its effect is accomplished by the stimulating action on the cardiovascular nervous system. The blood pressure sometimes is raised above that of the normal pressure for the individual. The effect lasts in normal persons for from two to three hours, that is, until the procaine solution is absorbed. In cases in which the block is ineffective the author advises a second infiltration two to three hours later. Bilateral infiltration is advisable in cases of low blood pressure and slow pulse or in cases in which unilateral block does not produce an improvement in blood pressure. Combination of vagus-sympathetic block with blood transfusion gives better results in traumatic shock than transfusion alone. Thus in shock of medium or grave degree transfusion of a liter of blood and of 270 cc. of substitute fluid gave on an average 25 mm. of mercury rise of blood pressure. In other words, for each 500 cc. of transfused blood there was a rise of blood pressure amounting to 10 mm. When the blood transfusion was combined with the vagus-sympathetic block the blood pressure in patients with shock, transfusion of 500 cc. of blood and 220 cc. of blood substitute gave an average rise of 22.5 mm. The effect of the block can be utilized not only in traumatic shock but in all states accompanied by collapse and hypoxia.

Vagus-Sympathetic Block.—According to Vishnevskiy, the physiologist Morrison called attention to the fact that section of the vagus nerve in the neck prevented the development of grave reflex manifestations on the part of respiration and cardiovascular function in the course of pneumonectomies in dogs. Vishnevskiy applied this principle in his operations on the human thorax. Instead of sectioning the nerve he utilized the method of creeping infiltration with a weak (0.25 per cent) solution of procaine hydrochloride. From 60 to 80 cc. of this solution is slowly injected at the edge of the sternocleidomastoid muscle above the point where it is crossed by the external jugular vein. The procaine solution slowly spreads and comes in contact with the perineural surfaces of the vagus, the sympathetic nerve and the phrenic nerve. The method proved to be very effective in the prophylaxis and therapy of pleural pulmonary shock. The author stresses the advantages of using a weak solution of procaine and its gradual penetration to the perineural tissues of the nerves.

Book Notices

Surgery of the Hand. By Sterling Bunnell, M.D. Cloth. Price, $12. Pp. 734, with 597 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1944.

This well written and beautifully illustrated monograph by America's foremost exponent of the surgery of the hand represents the work of a surgeon's lifetime. It obviously cannot be reviewed in adequate fashion in a few brief paragraphs. One should simply state that it deserves careful reading and study by every surgeon interested in the surgery of the upper extremity.

Although the title stresses the hand, it might have been "The Surgery of the Upper Extremity," for its scope is much broader than the simpler title indicates. The volume is divided into four parts. The first part includes a discussion of the comparative anatomy and a detailed description of the normal hand. Part 2 is devoted to the reconstruction of the hand and includes the subject of contractures, bone and joint disabilities, nerve and tendon injuries, and in a fifty page section on the arm in its relation to the hand subjects as diverse as sternoclavicular and acromioclavicular dislocations, recurrent dislocation of the shoulder, brachial plexus injuries and "tennis elbow." Part 3 is devoted to the treatment of injuries and infections of the hand and part 4 to congenital deformities, vasomotor and trophic conditions and to tumors, the latter section written by Dr. L. D. Howard Jr.

Part 2, devoted to the reconstruction of the hand and constituting approximately 380 of the 700 pages of the volume, describes the procedures which we have come to associate particularly with the author's name. Operations on the joints, nerve suture and the use of nerve grafts to fill defects, tendon suture and tendon grafting are described and illustrated in the clearcut fashion characteristic of the author's surgical papers. Because of the wealth of material presented and the many somewhat complicated technical procedures described it is difficult for a reviewer to choose any single subject or group of subjects and attempt to present the author's ideas or to evaluate them critically. One suggested procedure perhaps should be mentioned, both because of its importance and because it seems inconsistent with the admirable principle of "atraumatic technic" which the author has emphasized so forcefully. In discussing "débridement or excision of wound" (pp. 451-452) following injury of the hand, the author suggests that one ". . . sop the wound in all its interstices with a half-strength tincture of iodine as used on skin and then blot it dry at once to limit its action on the surface. This destroys surface bacteria and so marks the tissue that every particle can be excised. With toothed forceps and sharp plastic scissors (curved, flat and double pointed) the complete surface of the wound is systematically excised for 1 or 2 mm. deep, or more if necessary, to remove all nonviable tissue. First, the complete skin margin is excised, and circling deeper and deeper in the wound all is excised so completely in a dry and bloodless field that not a crumb of marked tissue remains. Exposed nerves, tendons, articular surfaces or essential structures are spared. The tendon and nerve ends are thinly clipped off, and ends of fractured bones are chiseled off to good bone. On completion we have a clean surgical wound lined with viable tissue free from bacteria, traumatized tissue and chemical." With a part of the body in which essential structures are packed so closely and lie so close to the surface, such a method of converting an open wound into a clean wound seems both ill considered and unnecessarily destructive.

One can say without exaggeration that no one heretofore has attempted so comprehensive or detailed a presentation of the surgical treatment of disabilities of the hand, and no surgeon who cares for such injuries or disabilities should fail to give this volume the considered attention it richly merits.

Crime and the Human Mind. By David Abrahamsen, M.D., Department of Psychiatry, Columbia University, New York. Cloth. Price, $3. Pp. 244. New York: Columbia University Press, 1944.

The claim that is made on the jacket of this book that this is the first volume to deal comprehensively with the psychiatric aspects of crime is untrue. Other books dating back to the end of the last century have been published on the subject, and many of them in their day were better than this one. True, Abrahamsen has brought under a single volume many of the more recent concepts of criminologic psychiatry, but his point of view seems to be extremely limited for a volume which has ten pages of bibliography. The author's point of view seems to be limited to a few of the most common articles on the subject having to do with criminologic psychiatry, and there is a preponderance of material coming from New York and perhaps an overemphasis on the reports of the Court of General Sessions Clinic.

The subject matter included in this volume deals with criminology as a science, the mind in relation to crime, heredity and environment as causes of crime—truly an unusual use of the word "cause"—the functional view of the offender, the psychiatric-psychologic examination of the offender, the psychology of the individual offender: classification, juvenile and war delinquency, the psychiatric-psychologic background of murder, the psychiatrist and the criminal law, and treatment and research.

Dr. Abrahamsen's career, as it is described on the jacket, would seem to give him an unusually fitting background to write a volume on psychiatry and crime, for he has been at St. Elizabeths Hospital in Washington, at the Illinois State Penitentiary and at the Psychiatric Clinic of the Court of General Sessions, but the book seems to be peculiarly unpractical. There are case histories given, but they lack the quality of reality. The bibliography too is peculiar. Little known works of rather insignificant authors on criminologic subjects are quoted, yet two or three psychiatrists who have contributed hundreds of articles to the literature, including several important monographs, are almost entirely ignored. In spite of these criticisms the book is interesting, carrying with it a limited amount of authenticity. Its use as a reference book, while limited, is justified and is definitely a step in the right direction of trying to make available for those who know little about it some phases of the relationship of crime to psychiatry.

Practical Methods in Biochemistry. By Frederick C. Koch, Director of Biochemical Research, Armour & Co., Chicago, and Martin E. Hanke, Associate Professor of Biochemistry, University of Chicago. Fourth edition. Cloth. Price, $2.25. Pp. 353, with 20 illustrations. Baltimore: William Wood & Company, 1943.

This edition presents the more important qualitative and quantitative aspects of cell constituents, of cell activities and of the composition of blood, secretions and excretions. The book is divided into three parts: (1) the chemistry of cell constituents, (2) the chemistry of the digestive tract and (3) blood and urine. Part 1 contains chapters dealing with carbohydrates, lipins, proteins and amino acids, nucleoproteins and nucleic acid, and hydrogen activity and p_H. Part 2 contains chapters devoted to salivary digestion, gastric digestion, intestinal digestion and bile. Part 3 has chapters on blood and hemoblobin, the quantitative analysis of blood, the quantitative analysis of urine, the chemical examination of urine for pathologic conditions, colorimetric methods for vitamins, and chemical tests for hormones. With each quantitative method are given the principle, the reagents and the actual procedure. The book could be considerably enriched by adding to each method a paragraph or two with biologic normals and clinical interpretations. The chapter on vitamins gives quantitative procedures for tissues and foods, but no such procedures for blood and for urine, which could have easily been incorporated. It is also to be regretted that spinal fluid is altogether left out of consideration. It is to be hoped that in the next edition clinical interpretations will be added as well as a chapter on spinal fluid, and that the chapters on vitamins and on hormones will be expanded to include quantitative methods for blood and urine.

The book is written in an exceptionally clear and fluent style, and the directions for various qualitative and quantitative procedures are simple, free from ambiguity and easy to follow. Explanations are freely used. The most valuable chapter in the book is the one discussing hydrogen activity and p_H. This subject is put before the student in the most illuminating manner, and the simple experiments in this chapter serve to illustrate fundamental principles. The superiority of the book lies in the choice of up-to-date subject matter. Many manuals published

continue to describe the same qualitative and quantitative procedures that have been used for thirty years or longer and fail to take into consideration new and more sensitive or more accurate methods. Koch and Hanke's book is replete to an agreeably surprising degree with the latest and best methods. Here is a book that is no longer a rehash of the old and the hoary in biochemical technic. Even the ordinary colorimeter has disappeared in the book to be altogether replaced by the more accurate photoelectric colorimeter, in which the personal equation is completely canceled out. The book is highly recommended and should be in the hands of every medical student, clinical pathologist and internist who desires to keep up with advances in the pure sciences intriguingly bound up with medical progress.

Elements of Electrocardiographic Interpretation with Forty Plates Illustrating the More Important Deviations from the Normal, Selected from the Files of the Michael Reese Hospital. By Louis N. Katz, A.M., M.D., Director of Cardiovascular Research, The Michael Reese Hospital, Chicago, and Victor Johnson, Ph.D., M.D. Third edition. Paper. Price, $1. Pp. 44, with 40 illustrations. Chicago: University of Chicago Press; London: Cambridge University Press, 1944.

P-Q-R-S-T: A Guide to the Interpretation of Electrocardiograms. By Joseph E. F. Riseman, M.D., Associate in Medicine, Harvard Medical School, Boston. Fabrikoid. Price, $1.50. Pp. 28, with 55 illustrations. Boston: The Author, 1944.

The value of the former booklet is established. The well chosen electrocardiograms, with adequate legends, illustrate the normal and abnormal mechanisms of the heart beat. "The Genesis of the Electrocardiogram" is new and helpful. Additions to the "Table of Characteristics of the Normal Electrocardiographic Cycle," plates illustrating the types and progressive changes of infarction and an illustrated discussion of chest leads are timely. The valuable "Procedure in Reading Electrocardiograms" is retained. The booklet provides useful supplementary material for students and practitioners.

The second booklet, of attractive format, is a detailed outline of graphic abnormalities (illustrated by drawings rather than actual electrocardiograms) and as such is of greatest value to the author.

The Safe Installation and Use of Abrasive Wheels. International Labour Office, Studies and Reports, Series F, Second Section (Safety), No. 9. Paper. Price, $1; 4s. Pp. 175, with illustrations. Washington & Montreal: International Labour Office; London: P. S. King & Staples, Ltd., 1944.

Grinders are exposed principally to injury arising from breakage of revolving abrasive wheels. Most commonly reported accidents are foreign bodies in the eye, burns and abrasions, or injury arising from contact with unprotected parts of the machine. This booklet, intended primarily for safety engineers, will, however, be a useful source of reference to physicians who encounter accidents of this type or who are called on to recommend improved health or safety measures. Complete data are presented about storage, proper wheels for particular work, speed of operation and stresses involved therein, mounting of the wheel and the precautions which workers must observe. Guarding receives exceptionally thorough treatment. Goggles or face screens need to be worn or transparent screens should be installed on the machine itself to protect the operator against sparks or dust. Local exhaust ventilation is regarded as the most reliable method of removing excessive concentrations of dust.

Rebel Without a Cause . . . The Hypnoanalysis of a Criminal Psychopath. By Robert M. Lindner, Ph.D., Psychologist, United States Penitentiary, Lewisburg, Pa. Introduction by Sheldon Glueck, LL.B., Ph.D., Professor of Criminal Law and Criminology, Law School, Harvard University, Boston, and Eleanor T. Glueck, Ed.D., Research Criminologist, Law School, Harvard University. Cloth. Price, $4. Pp. 296. New York: Grune & Stratton, 1944.

This entire book is written around the partial contents of forty-six hours of hypnoanalysis of a criminal psychopath. Preceding the single case report the author makes a few general remarks about the nature of psychopathic personalities and their evolution. To this subject his discussions add nothing new. The method of hypnoanalysis is then outlined and many current misconceptions are negated. In this discussion the positive contributions are worth studying, but the author's gratuitous ridicule of other methods is distracting. Then come 260 pages of case history and details of forty-six hours work. This is given in great detail, although of necessity abstracted to some degree. Page after page of the patient's production are cited with only an occasional question from the therapist. In the later hours the author became more curious and asked more questions and makes a few interpretations. One misses the analytic work of the therapist until the last hour, when a total explanation of the case is briefly given. This concerns a traumatic incident that occurred in infancy: "You were between 6 and 8 months old." The night before the child had been frightened by a dog in a motion picture. The next morning the patient saw his father having intercourse with the mother and his penis looked like a strange and vicious animal. The child knew he wasn't supposed to see all this. At breakfast he was frightened and cried. "Now the fear of your father's penis —and all it meant—followed you through all your life." To this traumatic incident the patient's lifelong nystagmus, amblyopia and ptosis and his psychopathy are attributed. The reviewer can make no comment regarding this claim except to point out that if a child of 6 months is able to grasp such a set of circumstances much indeed has been learned. A short summary follows in which the author states, "In short, hypnoanalysis is a radically abbreviated method for the investigation of the personality and the treatment of psychogenic disorders and aberrations of behavior."

Recent Advances in Anæsthesia and Analgesia (Including Oxygen Therapy). By C. Langton Hewer, M.B., B.S., D.A., Senior Anæsthetist, St. Bartholomew's Hospital, London. Fifth edition. Cloth. Price, $5.50. Pp. 343, with 141 illustrations. Philadelphia: Blakiston Company, 1944.

That a fifth edition of this invaluable manual should appear within two years of the publication of the fourth is a well merited tribute to its excellence. A good and fair description of "controlled respiration" has been added to the first chapter. The author has wisely modified his previous statement as to the effect of trichlorethylene on cardiac rhythm and now admits that arrhythmia occurs. A section dealing with wounds involving the mouth has been added to the chapter on anesthesia for oral operations, and anesthesia for thymectomy is considered in the chapter on thyroidectomy. A new chapter has been added on anesthetic charts and records, and the addition is timely and wise. To the professional anesthetist the book is indispensable because of the care and discrimination with which the references are selected, for the latter make the book a "starting point" for almost any investigation. In spite of the additions the book is not larger than before, and the printing and binding are astonishingly good in view of the prevailing restrictions. All anesthetists are indebted to Dr. Hewer's industry and learning for a work which is of vital importance to them.

The Art of Resuscitation. By Paluel J. Flagg, M.D., Chairman, Committee on Asphyxia, American Medical Association. Cloth. Price, $5. Pp. 453, with 176 illustrations. New York: Reinhold Publishing Corporation, 1944.

This volume, as the author states, is an attempt, based on more than twenty-five years of intimate experience with the unconscious patient, to tell the reader what to do when faced by an acutely asphyxiated patient about to die. The author has gathered together the essence of the papers that have been published on the subject of asphyxia and of resuscitation. He has spoken about it historically and from experimental and clinical points of view and has described asphyxia due to a variety of conditions and circumstances. His hobby, pneumatology, is described and recommended. He has covered asphyxia from the fetus to the death of the adult. There are a number of illustrations to assist in making his various points. An extensive bibliography precedes the index. Almost all methods of artificial respiration, both manual and mechanical, are illustrated. Most physicians should be more interested in artificial respiration than they are at present. The author emphasizes the important point that most physicians are not interested in artificial respiration and would prefer to call the fire department rather than to know how to do it themselves, and that this is an unhappy situation. He has done all he can to remedy this situation by preparing this book.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ETIOLOGY OF INFECTIOUS HEPATITIS FOLLOWING YELLOW FEVER VACCINE

To the Editor:—**In the literature on jaundice as caused by yellow fever vaccine which contained human serum, the latter has been said to be the probable source of the icterogenic virus or substance responsible for the hepatitis. Since human serum has been suspected in this connection, I am curious to know whether any similar increased incidence of infectious hepatitis has been noted in persons who have merely received transfusions of whole blood, especially during the subsequent three to twelve months interval? Would not such a statistical study decide definitely whether this icterogenic factor in serum was or was not at fault in the post-vaccinal jaundice?** **Captain, M. C., A. U. S.**

ANSWER.—There has not been any increase in the incidence of infectious hepatitis following transfusion of whole blood, or of serum or of plasma of similar magnitude to that following yellow fever vaccine. Studies of this incidence have not by themselves been conclusive in incriminating the normal serum which previously was included in yellow fever vaccine. There have been, however, some instances, with probable causal relationship, in which infectious hepatitis followed such transfusions after long intervals similar to those which occurred between injections of certain lots of yellow fever vaccine in 1942 and the appearance of jaundice. A possible explanation of the difference in incidence is that in the case of the yellow fever vaccine exceedingly small amounts of pooled normal human serum were used, around 0.04 cc. per dose: in such a small amount of serum an infecting dose of the hypothetical virus might be present without there being available an effective amount of accompanying specific antibodies which a larger dose of serum or blood would be likely to contain. Moreover, the very small amount of serum in the vaccine implies that a given icterogenic pool containing the serum of an infrequent human carrier would be distributed among thousands of doses of the vaccine. It has been noted also that certain pools of convalescent serum against mumps and measles, when given in considerable volume, produce numerous cases of infectious hepatitis, perhaps because they do not happen to contain an appreciable amount of specific antibody. In any event the evidence of the presence of an icterogenic virus in the blood of occasional human carriers is rapidly growing. The infection has been transferred to human volunteers by inoculation of serum in cases of postinoculation and other types of infectious hepatitis. Moreover, jaundice has ceased to appear in the large number of persons who have been vaccinated against yellow fever since serum was omitted in the manufacture of the vaccine. As susceptible species other than man have not been discovered, the proof of the etiology of postinoculation infectious hepatitis has not been completed by the isolation of the agent. Much, however, is already known about the supposed virus: it is filtrable and unusually resistant to heat, withstanding 56 C. for an hour.

LARGE DOSES OF ASCORBIC ACID

To the Editor:—**Can you give me any information as to the toxic effect of continued large doses of ascorbic acid (600 to 1,000 mg. daily)? An adult patient took up to 1,000 mg. of ascorbic acid daily on his own initiative for relief of hay fever. He observed that he was free from migraine headaches, which had previously occurred three or four times a month for almost fifteen years. The patient is anxious to know whether he can safely continue to take this large amount of ascorbic acid.** **M.D., New York.**

ANSWER.— There is little danger of harm resulting from large doses of vitamin C. Repeated doses of this vitamin have been administered to adults in amounts of 1 to 6 Gm. orally and intravenously without evidence of toxic action. Daily doses of 1 to 3 Gm. over an extended period caused no undesirable effect. In infants and children vagotonic effects such as fatigue, slow pulse, increased intestinal peristalsis and hyperemia have been noted with the use of maximal doses of vitamin C. This has been considered by some to be a sensitivity rather than a toxic manifestation.

The dose mentioned in the inquiry is not excessive and should cause no harmful effect.

SUBSTANCES USED TO INHIBIT CORROSION IN BOILERS

To the Editor:—**Is it safe to use "Corrodicide" or "Coravol" in hot water boilers from which steam goes to direct contact with food in pressure cookers? "Corrodicide" is supplied by the Metropolitan Refining Company of New York and "Coravol" is a product of the Western Chemical Company of Kansas City.** **Arthur E. Wade, M.D., Seattle.**

ANSWER.—Modern practice in the prevention of scaling and corrosion in boilers and hot and cold water systems makes use of a wide variety of organic and inorganic substances, including a small number of materials that may be volatilized and carried throughout the entire system along with steam. These inhibitor materials include zinc, manganese and chromium salts, soluble silicates such as sodium and ethyl, pyrophosphate, hexametaphosphate, sodium septaphosphate, trisodium and disodium phosphate, sodium carbonate and amines. Not all of these substances reach foods subjected to pressure and heat from steam created in a boiler containing these substances. Many appliances, such as steam tables, produce heat or steam without any direct connection with the steam generated in the primary boilers. Whenever practical, that type of device making use of secondary systems is preferred. Frequently claims are made that corrosion inhibitors are nonvolatile and therefore never reach steam. Theoretically, at least, many substances labeled as nonevaporable are carried along with steam. This is well exemplified in the necessity for triple distillation of distilled water for certain highly technical purposes.

The two substances specified in the query are chemically highly dissimilar. "Corrodicide" primarily is intended for use in hot or cold water supply systems and not in boilers. The formula for this inhibitor is not fixed but is based on the analysis of the particular water to be treated. The formula commonly includes trisodium phosphate, disodium phosphate, sodium carbonate and sodium silicate. None of these substances are toxic in small quantities. However, its manufacturers produce and market another inhibitor, named "Corrodine," which is a volatile liquid and which might reach pressure cookers. This material is introduced into boilers but is not specified by the manufacturer for use when steam comes in contact with foodstuffs.

"Coravol," a volatile substance and intended for the lines of the system only, represents one or more amines. The nature of the application of "Coravol" is such that, in small quantities, foods in pressure cookers directly connected with boilers making use of this inhibitor and persons in such steamy atmospheres may be in the presence of traces of this amine or these amines. It is probable that due safeguards already have been provided. Any foods cooked in the presence of abnormal quanities of this amine would not be sapid nor would water be potable. Moreover, the quantity requisite to adequate anticorrosion purposes is so low that any quantity escaping into a pressure cooker or into the atmosphere under normal operating conditions would be so low that injurious effects would be unlikely. In short, when dangerous quantities might be present, odor and taste would serve as warnings. Not all amines possess offensive odors, as is well attested through common experience of users of many brands of brushless shaving creams, which substances contain amines. On the other hand, the highly offensive odors of decomposing fish are partly due to the putrefactive formation of trimethylamine. Some amines also are skin irritants, such as the well known paraphenylenediamine, the much used photosensitive fur dye.

It appears that "Corrodicide" is not sponsored by its manufacturers for steam systems and therefore when properly used may be ruled out as a source of prospective injury under the circumstances of the inquiry. "Coravol," an amine or mixture of amines, is a caustic skin irritant in high concentration and a convulsive poison after hypodermic introduction in such quantities as 0.5 Gm. per kilogram of body weight. It appears to be lacking in dangerous properties when administered by mouth in dilution in such doses as 100 mg. per kilogram of body weight daily. Such quantities under normal usage of "Coravol" are unlikely to reach food or food workers. Moreover, any accidental major exposures probably would be accompanied by disturbing odors and tastes.

Both of the manufacturers concerned cooperated in furnishing information conducive to the proper appraisal of this problem.

References:

Dreyfus, M. E.: Controlling Corrosion in Steam and Return Lines, *Power Plant Engin.*, April 1938, p. 274.

Dreyfus, M. E.: The Application of Organic Amines to Steam Systems, *Heat. & Vent.*, June 1942, p. 31.

EXERCISES FOR RELIEF OF DYSMENORRHEA

To the Editor:—There have been recent reports of the large scale use of the so-called Billig exercise for dysmenorrhea and of the extremely favorable results of its practice at the University of California, in the Los Angeles City School System, in the Consolidated Vultee Aircraft Corporation and elsewhere. A report in the September 1943 issue of *Industrial Medicine* by A. C. Dick and others gives the following explanation regarding the exercise: "Treatment is based on the discovery that in women with dysmenorrhea there is a postural defect of contracted fascial ligamentous bands restricting posterior tilt excursion range of the pelvis in relation to the legs and back. At menstruation (with the change in ovarian hormone level) the ligaments further shorten, causing impingement with irritation of the peripheral spinal nerves passing through and by them. The nerves usually irritated are one or more of the following: 11th dorsal, 12th dorsal, 1st lumbar and their branches, the ilioinguinal and iliohypogastric. The impingement gives rise to symptoms of pain in the low back in the region of irritation or in the region of distribution of these nerves in the lower abdominal wall and groin, or both. Factors influencing the contracture of the ligaments are varied. Treatment consists in freeing the nerves of their impingement by correcting the postural defect. This is done through precise ligamentous stretching exercises carried out by the patient routinely to progressively, accumulatively lengthening the ligaments involved." The Harlan Shoemaker Fund for Paralytics furnishes a 16 mm. film of the exercise and is apparently sponsoring similar exercises for other painful conditions. Is the explanation offered of the mechanics of menstrual pain and its alleviation by exercise physiologically acceptable? Is there any corroborating evidence of the value of such an exercise?

M.D., New York.

ANSWER.—It has not been proved that in all or most women with primary dysmenorrhea "there is a postural defect of contracted fascial ligamentous bands restricting posterior tilt excursion range of the fibers. . . ." Likewise there is no proof that at menstruation the ligaments further shorten, impinge and irritate the peripheral spinal nerves enumerated in the query. Furthermore, it has not been shown that there is any connection between impingement and irritation of the peripheral spinal nerves and dysmenorrhea. The part of the nervous system which is definitely associated with painful menstruation is the sympathetic nervous system, particularly the part usually referred to as the presacral nerves. The operation of presacral neurectomy has relieved the vast majority of patients with dysmenorrhea for whom it has been tried.

H. E. Billig Jr. (*Arch. Surg.* **46**:611 [May] 1943) and A. C. Dick, H. E. Billig Jr. and H. N. Macey (*Indust. Med.* **12**:588 [Sept.] 1943) claim excellent results in cases of dysmenorrhea from the use of the special exercises. During the first ten months of installation of the exercises 70,000 absentee hours were eliminated and there was an 80 per cent reduction in the use of menstrual cramps as an absentee excuse. Also 70,000 decreased efficiency hours were eliminated. Another favorable report was written by Esther Gilman (*J. Health & Phys. Educ.* **15**:377 [Sept.] 1944). In view of the favorable results described, if there was not a large psychic factor involved, some other reason for the benefits must be sought than that given by the proponents.

LEUKOCYTE PICTURE IN MALARIA

To the Editor:—In this Carolina coast town, we have a certain amount of malaria, both acute and chronic. This summer, in the laboratory, we have obtained a series of blood counts like this: There is usually an increased total number of white cells, running about twelve or thirteen thousand; in the differential Schilling count, there is a high proportion of young cells, running as high as 30 per cent of the total number of polymorphonuclear cells counted; the overall total of the polymorphonuclear cells is little or not at all above the normal 70 per cent; there may be definite increase to around 30 to 40 per cent in the lymphocyte series. With this count we frequently find plasmodia. These patients usually have slight or definite fever and usually complain of dizziness and malaise, but they are not particularly toxic. They definitely are not as sick as one would expect from the pronounced shift to the left as seen in severe infections. Has this sort of blood count been noticed by other workers in the field of malaria diagnosis?

Joseph R. Latham, M.D., New Bern, N. C.

ANSWER.—The characteristic white blood cell picture in acute malaria consists in an increased total count during the actual onset, but as soon as the attack reaches its maximum, either clinically or by the appearance of an increased number of infected red blood cells, and thereafter to and during the quiescent interval until the next onset, the count decreases to normal or even to 5,000 or less. In chronic malaria there is usually a leukopenia, with a deficiency in the neutrophils. Almost invariably there is a monocytosis, with an increase in the number of monocytes and lymphocytes, and in acute infections there may be an appreciable number of wandering histiocytes.

American and British textbooks make no specific mention of the Schilling count, but Mühlens, Nauch, Vogel and Ruge (Krankheiten und Higiene der warmen Länder, ed. 4, Leipzig, Georg Thieme, 1938, p. 82) state that during attacks there is a shift to the left in the Schilling count, as observed by V. Schilling himself (1924), with the appearance of juvenile forms and metamyelocytes. Moreover, Böhm (1918), Newham and Duncan (1924) and Beregoff (1934) have also observed stab or band forms in severe infections; Winfield (1932) has reported a shift to immature stages proportional to the severity of the disease. Schilling found that even between attacks, when the neutrophils were greatly diminished, stab forms might still be present, indicating a severe drain on the granulocyte-forming tissues.

In severe infections both monocytes and mature neutrophils frequently have ingested malaria pigment and parasites of all stages. Owing to increased phagocytic activity of the large monocytes and a consequent increase in their production, the proportion of these cells to the total white cells may reach 30 per cent. In the absence of other diseases of the blood stream and blood-forming organs, a monocytosis of 15 to 20 per cent with an associated leukopenia is suggestive of malaria, while 8 per cent or less of large monocytes is presumptive evidence of freedom from malaria.

Although there is considerable difference in individual observations, the following changes in the white blood cell picture are characteristic of malaria: there is a relative and sometimes an absolute increase in the number of large monocytes. There may be a leukocytosis, particularly if the discharge of parasites from destroyed red blood corpuscles is heavy; but if the parasites are scant there may be no increment in the total number of white cells. Usually, but not invariably, the periods between attacks are characterized by leukopenia with monocytosis.

PENICILLIN FOR SCARLET FEVER

To the Editor:—A healthy white boy aged 6 years contracted fairly severe scarlet fever with rectal temperatures reaching 104 to 106 F. on the fourth day, pronounced asthenia and severe multiple synovitis. Since the onset he had been given adequate doses of sulfadiazine and small doses of acetylsalicylic acid for the control of the fever and the arthralgias. The parents refused serum "because it harms the heart." On the fourth day after the appearance of the rash I decided to suspend all other medication and injected 5,000 units of penicillin every three hours. After the second injection the fever started to diminish and the boy's temperature became normal the following day. But the most surprising effect was that on his joint pains; these seemed to disappear under the influence of the penicillin. I realize that care must be taken in order to avoid "post hoc ergo propter hoc" judgment. However, my understanding is that the temperature in scarlet fever does not return to normal by crisis but by lysis, and in this instance it returned by crisis. On the other hand, I do not believe that the high fever could be attributed, even partly, to the sulfadiazine, because the patient kept on taking it during the fourth day, in spite of my order to stop it, and yet the temperature went down. Aside from some traces of albumin, the urine was normal all the time. The diagnosis of scarlet fever in this patient was established firmly. As far as I know, penicillin has not been used in scarlet fever so far.

Mardoqueo I. Salomon, M.D., Bronx, New York.

ANSWER.—It is unusual for a scarlet fever patient to develop multiple synovitis as early as the fourth day of the disease. In the presence of such a complication one would be justified in prescribing sulfadiazine, which, however, is of little or no value for subduing the toxemia of scarlet fever. Although the dosage of sulfadiazine is not stated, it does not seem probable that this drug was responsible for the elevated temperature in the case discussed. Following the administration of scarlet fever antitoxin or human convalescent scarlet fever serum, the temperature commonly falls by crisis. At present, scarlet fever in general is exceptionally mild and has been so for the last few years. Possibly on that account penicillin has been somewhat neglected for this infection. However, penicillin has been given successfully for the treatment of complications of scarlet fever.

ROTARY NYSTAGMUS

To the Editor:—The reply to an inquiry about rotary nystagmus published in The Journal, Jan. 27, 1945, page 252, concerned a Negro woman aged 42 who had rotary nystagmus of uncertain duration, possibly about twenty-five years, and who had no other symptoms. The reply stated that rotary nystagmus may be congenital and that it occurs in defective vision and ocular muscle weakness. On the contrary, in these conditions the nystagmus is horizontal, not rotary. Rotary nystagmus does occur in acute conditions of the inner ear, as stated in the reply, but is of short duration and is accompanied by vertigo, conditions specifically eliminated in the query. Finally, the statement that rotary nystagmus is not a sign of organic disease of the central nervous system is questionable. It is an excellent sign of such disease. The isolated finding of rotary nystagmus probably indicates a small lesion in the vestibular or vestibulocerebellar tracts or their nuclei. In the absence of other findings one cannot say more. If old, it may be residual of a small inflammatory lesion. If recent, one might suspect the presence of a plaque of disseminated sclerosis.

C. Wilbur Rucker, M.D., Rochester, Minn.